

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Continued Prosecution Application

Under 37 C.F.R. § 1.53(d) Based On:

Application of: LeCluyse, Edward L., et al. Group Art Unit: 1651

Serial No.: 09/527,352 Examiner: Afremova, V.

Filed: March 17, 2000 Docket No.: 421/17/2

For: METHOD OF SCREENING CANDIDATE COMPOUNDS FOR

SUSCEPTIBILITY TO BILIARY EXCRETION

DECLARATION OF XINGRONG LIU PURSUANT TO 37 C.F.R. §1:132

Commissioner of Patents P. O. Box 1450 Alexandria, VA 22313-1450

Sir:

- 1. I, Xingrong Liu, am a co-inventor of the invention disclosed and claimed in the subject above captioned U.S. Patent Application Serial No. 09/527,352 and the sole author of the dissertation entitled, "Sandwich-Cultured Rat Hepatocytes: A Novel In Vitro Model To Study Hepatobiliary Disposition Of Substrates", filed with the U.S. Patent and Trademark Office in a supplemental filing dated May 28, 2003 and marked therein as "Exhibit B" (hereinafter the "Dissertation").
- 2. The Dissertation was written and submitted by me to the University of North Carolina at Chapel Hill in partial fulfillment of criteria for my Ph.D. degree. As such, I am listed as the sole author of the Dissertation.

- My co-inventors on the present U.S. Patent Application Serial No. 3. 09/527,352, Drs. Kim Brouwer and Edward LeCluyse, provided input, support and guidance to the underlying research set forth in the Dissertation, and also provided editorial assistance in drafting and organizing the Disseration. However, given that the Dissertation was prepared in partial fulfillment of criteria for my Ph.D. degree, Drs. Brouwer and LeCluyse were not identified as co-authors of the Dissertation.
- Co-inventors, Liu, Brouwer, and LeCluyse, are the sole co-inventors of the subject matter disclosed in the Dissertation and which is also part of the subject matter disclosed in the subject U.S. Patent Application Serial No. 09/527,352.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Man 3, 2004



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Under 37 C.F.R. § 1.53(d) Based On:

Application of: LeCluyse, Edward L., et al.

Group Art Unit: 1651

Serial No.: 09/527,352

Examiner: Afremova, V.

Filed: March 17, 2000

Docket No.: 421/17/2

For: METHOD OF SCREENING CANDIDATE COMPOUNDS FOR

SUSCEPTIBILITY TO BILIARY EXCRETION

DECLARATION OF RONALD T. BORCHARDT, PH.D PURSUANT TO 37 C.F.R. §§1.132

Commissioner of Patents Washington, D.C. 20231

Sir:

- 1. My name is Ronald T. Borchardt, Ph.D., and I am currently Solon E. Summerfield Distinguished Professor In the Department of Pharmaceutical Chemistry at the University of Kansas. I am also on the Scientific Advisory Board and Board of Directors of Qualyst, Inc.
- 2. A true and accurate copy of my *curriculum vitae*, which evidences my expertise and credentials, is attached herewith and labeled **Exhibit A**.
- 3. I have had an opportunity to review pending claims 105-118 in the subject above captioned U.S. Patent Application Serial No. 09/527,352.
- 4. I have also reviewed the following documents: the Official Action issued January 2, 2004 on the above captioned U.S. Patent Application Serial No. 09/527,352 by the U.S. Patent and Trademark Office; and <u>Liu et al.</u> (1997) *Pharm.* Res. 24:S-459 (hereinafter referred to as <u>Liu et al. [EE]</u>) cited in the Official Action.

- 5. <u>Liu et al. [EE]</u> describes calculating a biliary excretion index based on the difference in retention of substrate in standard buffer compared to calcium-free buffer at 10 minutes in Day 5 sandwich-cultured hepatocytes.
- 6. A biliary clearance value, as described in the present U.S. patent application, is calculated from fundamentally different data than those required for calculating the biliary excretion index. In order to collect these data, a different experimental design is required. The biliary excretion index is calculated from the difference in substrate accumulation between standard and calcium-free buffer. This difference (i.e., the mass of substrate that appears in the bile) comprises the numerator in both the biliary excretion index and the billary clearance value calculation. However, the denominator differs for these two parameters. For the biliary excretion index, the denominator is simply substrate uptake in standard buffer. In contrast, for determination of a biliary clearance value, the area under the curve (AUC), wherein the AUC represents the integral of xenobiotic concentration in the medium from time 0 to time T, serves as the denominator in the biliary clearance calculation.
- 7. There is no disclosure in the <u>Liu et al. [EE]</u> abstract of any experimental design in which the calculation of AUC could be accomplished. Without this requisite information, biliary clearance cannot be calculated.
- 8. The billary excretion index only reflects the fraction of the substrate accumulated in the hepatocyte that ultimately is excreted into bile. In essence, this parameter indicates the disposition of a compound only after it has been taken up into the cell. In contrast, the billary clearance value determines the rate at which a compound will move from outside the cell into bile, without respect to which step (net uptake by the cell or movement from the cell interior into bile) might be the rate-limiting process. The distinction between the utility of the billiary excretion index and the billiary clearance value is important. A compound may have a high billiary excretion index even if billiary excretion is not an important route of elimination from the body. For some compounds, net uptake by the hepatocyte may be low (due to low uptake or significant efflux from the cell into the media), so that the liver does not contribute significantly to overall removal of the compound from the body. However, excretion of the compound from the cell into bile may be efficient. In this case, the

biliary excretion index would be high, even though biliary excretion, from a biologic standpoint, would be unimportant. In contrast, the biliary clearance value would accurately characterize the behavior of the compound: a low degree of uptake into the hepatocyte will yield a low measure of biliary clearance regardless of how efficiently the compound is removed from the cell into bile.

- 9. Physiological processes, such as clearance values, are additive and typically scale across species. This is not necessarily true for fractional excretion values. Compounds usually are categorized as low, intermediate or high clearance. Total body clearance is the sum of hepatic clearance and clearance by all non-hepatic routes; in turn, hepatic clearance is the sum of metabolic clearance and biliary clearance. Total body clearance is a determinant of compound concentrations in blood that are produced by a given administration regimen for that compound. Hepatic clearance is a further determinant of systemic concentrations for compounds that are administered orally (as are most therapeutic agents) in that hepatic clearance can mediate loss of the compound before it appears in the systemic circulation (so-called "first-pass extraction" by the liver). It is critically important to identify compounds (potential drugs) that have a high hepatic clearance, as these will suffer a high degree of first-pass loss (and therefore may be undesirable as therapeutic agents). Compounds that have a high biliary clearance will have a high hepatic clearance and therefore, a large first-pass extraction; compounds with a high biliary excretion index may or may not have a high hepatic clearance.
- 10. The utility of the *in vitro* biliary clearance value, but inability of biliary excretion index, to predict *in vivo* biliary clearance is evident in the data submitted in the subject U.S. Patent Application Serial No. 09/527,352. See for example, Figures 6A and 6B. In Figure 6A, the biliary excretion index of methotrexate (open circle) is relatively high. However, the low *in vivo* biliary clearance value of methotrexate, as shown in Figure 6B of the subject U.S. Patent Application Serial No. 09/527,352, indicates that as methotrexate moves through the liver on any single pass, it is not rapidly or extensively excreted into bile. This can be the case if methotrexate is cleared predominantly by another route of elimination *in vivo* (e.g., non-hepatic

routes). Biliary clearance also can be low if methotrexate is not taken up efficiently by the hepatocyte. Thus, the susceptibility of methotrexate to biliary excretion is low, but this would not be predicted by the biliary excretion index. In contrast, the low in vitro biliary clearance of methotrexate determined in the sandwich-cultured hepatocytes is predictive of the *in vivo* biliary clearance value.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Ronald T. Borchardt, Ph.D

3/26/04

Date

Attachment: Exhibit A



Curriculum Vita Ronald T. Borchardt

Solon E. Summerfield Distinguished Professor of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS

Address:

Business

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Personal Information: Born: February 18, 1944

Marital Status: Married

Wife: Pamela K.

Children: Scott R., Paul M., Kelly C.

Education:

Year

Scientific

Home

3100 Campfire Drive

(785) 842-5075

Lawrence, Kansas 66049

Institution and Location

Degree

Conferred Field

School of Pharmacy, University of

Wisconsin, Madison, Wisconsin

B.S.

1967 Pharmacy

School of Pharmacy, University of

Kansas, Lawrence, Kansas Ph.D.

D. 1970

Medicinal Chemistry

NIH, NIAMD, Bethesda, Maryland

Postdoc.

1971 Physical Organic Chemistry

Research and Professional Experience:

1983-present:

Solon E. Summerfield Distinguished Professor, Department of Pharmaceutical Chemistry, The

University of Kansas

1983-1998:

Victorian Professor, Victorian College of Pharmacy, Melbourne, Australia

1983-1998:

Chairman, Department of Pharmaceutical Chemistry, The University of Kansas

1981-1999:

Solon E. Summerfield Distinguished Professor, Department of Molecular Biosciences, The University

of Kansas

1981-1994:

Solon E. Summerfield Distinguished Professor, Department of Medicinal Chemistry, The University

of Kansas

1991-1993:

Acting Dean, School of Pharmacy, The University of Kansas

1981-1988:

Director, The Center for Biomedical Research, The University of Kansas

1979-1981:

Professor, Department of Biochemistry, The University of Kansas

1974-1979:

Established Investigator of the American Heart Association

1975-1979:

Associate Professor, Department of Biochemistry, The University of Kansas

1971-1975:

Assistant Professor, Department of Biochemistry, The University of Kansas

1969-1971:

Senior Assistant Scientist, Laboratory of Chemistry, National Institute of Arthritis and Metabolic

Diseases

1967-1969:

NSF Graduate Fellow, Department of Medicinal Chemistry, School of Pharmacy, The University of

Kansas

Membership on Scientific and Educational Advisory Committees:

1976-1979:	American Heart Association, Kansas Affiliate Research Review Committee, member
1979-1981:	American Heart Association, Kansas Affiliate, Research Review Committee, Chairman
1977-1981:	American Heart Association, Midwest Regional Research Review Committee, member
1980-1984:	Pharmacological Sciences Review Committee, National Institute of General Medical Sciences, member
1986-1988:	Cancer Therapeutics Program Project Review Committee, National Cancer Institute, member
1987-1993:	Advisory Committee, George Herbert Hitchings Award for Innovative Methods in Drug Design, The Burroughs Wellcome Fund, member
1992-1994:	Scientific Advisory Board, Oread Laboratories, Chairman
1996-1999:	Scientific and Technical Advisory Board, Oread Inc., Chairman
1996-2001:	Scientific Advisory Board, NaviCyte, Inc.
1999-2001:	Scientific Advisory Board, Coelacanth Corporation
1996-2002:	Scientific Advisory Board, AvMax Corporation
2000-2003:	Research Committee, American Heart Association, Heart Land Affiliate
1987-present:	Advisory Committee, International Sato Memorial Award-The Foundation for Advanced Education in the Sciences, Inc., Chairman
1996-present:	Scientific Advisory Board, West Pharmaceutical Services
1996-present:	Board of Directors, Globalization of Pharmaceutics Education Network
1996-present:	Executive Committee, Globalization of Pharmaceutics Education Network
1997-present:	Scientific Advisory Board, Arizeke Pharmaceuticals, Inc.
1997-present:	Scientific Advisory Board, ProQuest Pharmaceuticals, Inc.
1999-present:	Scientific Advisory Board, Guilford Pharmaceuticals, Inc.
2000-present:	Scientific Advisory Board, Diazyme Laboratories
2000-present:	Drug Development Advisory Board, Scios, Inc.
2000-present:	Scientific Advisory Board, Pointilliste, Inc.
2001-present:	Scientific Advisory Board, Ricerca, LLC
2001-present:	Scientific Advisory Board, Lexicon Pharmaceuticals, Inc.
2001-present:	Scientific Advisory Board, Argolyn Bioscience, Inc.
2002-present:	Scientific Advisory Board, Roche Palo Alto
2002-present:	Scientific Advisory Board, Eiffel Technologies
2003-present:	Scientific Advisory Board, Absorption Systems
2003-present:	Scientific Advisory Board, Enzon Corporation
2003-present:	Pharmaceutical R&D Advisory Board, Abbott Laboratories
2003-present:	Board of Directors and Scientific Advisory Board, Qualyst, Inc.

Membership in Professional Organizations (Present):

American Chemical Society, Medicinal Chemistry Section
American Society for Pharmacology and Experimental Therapeutics
American Society for Biochemistry and Molecular Biology
American Association for the Advancement of Science
American Association of Pharmaceutical Scientists
American Society for Cell Biology
The Protein Society
International Society for Antiviral Research
American Peptide Society
American Pharmaceutical Association
American Association of Colleges of Pharmacy
European Federation for Pharmaceutical Sciences

Editorships

Series Editor, Pharmaceutical Biotechnology (Kluwer/Plenum), 1989-2001
Associate Editor, Journal of Pharmaceutical Sciences, 1996-2001
Associate Editor, Journal of Peptide Research, 1998-2001
Editor (Biotechnology), AAPSPharmSci, 1999-2001
Series Editor, Biotechnology: Pharmaceutical Aspects (AAPS Press), 2001-present Editor, Journal of Pharmaceutical Sciences, 2001-present

Editorial Boards:

Journal of Medicinal Chemistry - 1988-1993
Antiviral Research - 1988-2000
AAPSPharmSci - 1999-2001
Journal of Peptide Research - 1997-2001
European Journal of Pharmaceutical Sciences - 1998-2003
Pharmaceutical Research - 1986-present
Journal of Drug Targeting - 1992-present
Advanced Drug Delivery Reviews - 1992-present
Perspective in Drug Discovery and Design - 1992-present
Journal of Pharmaceutical Sciences - 1994-present
Molecular Interventions - 2000-present

Editorial Activities (Present):

Ad Hoc Reviewer for the Journal of Medicinal Chemistry, Journal of Organic Chemistry, Biochemistry, Molecular Pharmacology, Biochemical Pharmacology, Journal of Biological Chemistry, Biochimica et Biophysica Acta, Journal of the American Chemical Society, Analytical Biochemistry, Life Sciences, Science, Journal of Pharmacology and Experimental Therapeutics, Journal of Bacteriology, Archives of Biochemistry and Biophysics, Proceedings of the National Academy of Science, Journal Neurochemistry, International Journal of Pharmaceutics, Journal of Pharmaceutical Sciences, Nucleosides and Nucleotides, Pharmaceutical Research, Cancer Research, Bioorganic and Medicinal Chemistry Letters, AAPSPharmSci

Committee Activities (Present):

- 1. University or Departmental
 - (a) Biochemical Service Research Laboratory Steering Committee University
 - (b) NCI Bioanalytical Training Grant Steering Committee University
 - (c) NIGMS Biotechnology Grant Steering Committee, Chairman University
- 2. Outside Research and Public Service
 - (a) Ad Hoc Reviewer for National Science Foundation and National Institutes of Health

Consultantships:

INTERx Corporation, Lawrence, KS, 1971-1981

Merck, Sharp & Dohme, Rahway, NJ, 1981-1986

Glaxo, Inc., Research Triangle Park, NC, 1986-1995

Oread Laboratories, Lawrence, KS, 1992-1994

Wyeth-Ayerst Pharmaceuticals, 1994

Whitehall-Robins Pharmaceuticals, 1995

Affymax Corporation, Palo Alto, CA, 1995-1998

Tanabe Research Laboratories, San Diego, CA, 1997-1999

Oread Inc., Lawrence, KS, 1996-1999 (Chairman of the Scientific and Technical Advisory Board)

Rhone-Poulenc Rorer, Collegeville, PA, 1993-1999

Hoechst Marion Roussel, Kansas City, MO, 1994-1999

Alza Corporation, Palo Alto, CA, 1993-1999

Astra-Zeneca Pharmaceuticals, Inc., Wilmington, DE, 1995-2001

NaviCyte, Inc., San Diego, CA, 1996-2001 (Member of the Scientific Advisory Board)

Biogen Corporation, Cambridge, MA, 1997-2001

COR Therapeutics, Inc., South San Francisco, CA, 2000-2002

Wyeth-Ayerst Research, Cambridge, MA, 2000-2002

Vertex Pharmaceuticals, Inc., Cambridge, MA, 1997-2002

AvMax, Inc., Belvedere, CA, 1995-2002 (Member of the Scientific Advisory Board)

ARIAD Pharmaceuticals, Cambridge, MA, 1998-2002

Inhale Therapeutic Systems, San Carlos, CA, 2001-2002

Pharmacia, Inc., Kalamazoo, MI, Skokie, IL, and Chesterfield, MO, 1983-2003

GlaxoSmithKline Pharmaceuticals, Upper Marion, PA, 1993-present

Genentech Corporation, South San Francisco, CA, 1993-present

West Pharmaceutical Services, Lionville, PA, 1996-present (Consultant and Member of the Scientific Advisory Board)

Arizeke Pharmaceuticals, Inc., Del Mar, CA, 1997-present (Consultant and Member of Scientific Advisory Board)

ProQuest Pharmaceuticals, Inc., Lawrence, KS, 1997-present (Founder, Consultant and Member of Scientific Advisory Board)

Hoffmann-LaRoche, Inc., Nutley, NJ, 1998-present

Millennium Pharmaceuticals, Inc., Cambridge, MA, 1998-present

Guilford Pharmaceuticals, Inc., Baltimore, MD, 1999-present (Consultant and Member of the Scientific Advisory Board)

Serono Reproductive Biology Institute, Inc., Randolph, MA and Geneva, Switzerland, 1999-present

Aventis Corp., Bridgewater, NJ and Frankfurt, Germany, 1999-present

Diazyme Laboratories, San Diego, CA, 2000-present (Consultant and Member of Scientific Advisory Board)

Pointilliste, Inc., Mountain View, CA, 2000-present (Consultant and Member of Scientific Advisory Board)

Ricerca, LLC, Painesville, OH, 2001-present (Consultant and Member of Scientific Advisory Board)

Lexicon Pharmaceuticals, Inc., East Windsor, NJ, 2001-present (Consultant and Member of Scientific Advisory Board)

Roche-Palo Alto, Palo Alto, CA, 2001-present (Consultant and Member of Scientific Advisory Board)

Sepracor, Inc., Marlborough, MA, 2001-present

Argolyn Bioscience, Inc., Charleston, SC, 2001-present (Consultant and Member of Scientific Advisory Board)

3D Pharmaceuticals, Exton, PA, 2002-present

Synaptic Corporation, Parnas, NJ, 2002-present

Metaphore Pharmaceuticals, Inc., St. Louis, MO, 2002-present

Eiffel Technologies, Melbourne, Australia (Consultant and Member of Scientific Advisory Board), 2002-present

Infinity Pharmaceuticals, Inc., Cambridge, MA, 2002-present

AstraZeneca, Waltham, MA, 2003-present

Concurrent Pharmaceuticals, Fort Washington, PA, 2003-present

Sunesis Pharmaceuticals, Inc., South San Francisco, CA, 2003-present

Genomics Institute of the Novartis Research Foundation, San Diego, CA, 2003-present

Artesian Therapeutics, Gaithersburg, MD, 2003-present

Rib-X Pharmaceuticals, New Haven, CT, 2003-present

Abbott Laboratories, Abbott Park, IL (Consultant and member of the Pharmaceutical R&D Advisory Board), 2003-present

Enzon Corporation, Bridgewater, NJ (Member of Scientific Advisory Board), 2003-present

Qualyst, Inc., Raleigh, NC (Consultant and Member of Scientific Advisory Board), 2003-present

Absorption Systems, Exton, PA (Consultant and Member of Scientific Advisory Board), 2003-present

Neurocrine Biosciences, Inc., San Diego, CA (), 2003-present

Honors:

- Established Investigator of the American Heart Association, 1974-1979
- Elected to Membership in the American Society of Pharmacology and Experimental Therapeutics, 1974
- Elected to Membership in the American Society of Biochemistry and Molecular Biology, 1977
- Mortar Board Outstanding Educator, The University of Kansas, 1980
- E. C. Franklin Lecturer University of Kansas, 1980
- Mid-America State Universities Association (MASUA) Honor Lecturer, 1980-1981
- Sato Memorial International Award Pharmaceutical Society of Japan and the Foundation for Advanced Education in the Sciences, 1981
- Named Solon E. Summerfield Distinguished Professor of Biochemistry University of Kansas, 1981
- Dolph C. Simons, Sr. Research Award in the Biomedical Sciences University of Kansas, 1983
- Elected to Membership in the American Society for Cell Biology, 1985
- J. Clarence Karcher Lecturer, University of Oklahoma, 1988
- Parke-Davis Distinguished Lecturer, Rutgers University, 1988
- Fellow, American Association of Pharmaceutical Scientists, 1988
- Minnetonka Lecturer, University of Minnesota, 1989
- Citation of Merit, University of Wisconsin-Madison, 1989
- Percy L. Julian Sigma Xi Lecturer, Howard University, 1991
- Meritorious Manuscript Award, American Association of Pharmaceutical Scientists, 1991
- Watkins Visiting Professorship in the Life Sciences, Wichita State University, 1992
- Kenneth E. Avis Distinguished Visiting Professor, The University of Tennessee-Memphis, 1993
- Takeru and Aya Higuchi Memorial Award, Academy of Pharmaceutical Sciences and Technology, Japan, 1993
- Research Achievement Award in Biotechnology, American Association of Pharmaceutical Scientists, 1993
- 14th Annual Graduate Student Symposium for the Pharmacological Sciences Keynote Speaker, University of Michigan, 1994
- Distinguished Lecturer, University of Kentucky, 1994
- Research Achievement Award in Medicinal Chemistry and Natural Products Chemistry, American Association of Pharmaceutical Scientists, 1994
- Fellow, American Association for the Advancement of Science, 1995
- David Guttman Lecturer, University of Kentucky, 1997
- Paul Dawson Biotechnology Award, American Association of Colleges of Pharmacy, 1997
- Louis Byrd Graduate Educator Award, The University of Kansas, 1997
- Distinguished Pharmaceutical Scientist Award, American Association of Pharmaceutical Scientists, 1997
- Wellcome Visiting Professor in the Basic Medical Sciences, Washington State University, 1998
- Volwiler Research Achievement Award, American Association of Colleges of Pharmacy, 1998
- Meritorious Manuscript Award, American Association of Pharmaceutical Scientists, 1998
- Host-Madsen Medal, Federation Internationale Pharmaceutique, 1999
- Distinguished Service Award FASEB Research Conference on Biological Methylation, 1999
- Millennial Pharmaceutical Scientist Award, The Millennial World Congress of Pharmaceutical Sciences, April, 2000
- Leiden/Amsterdam Center for Drug Research Distinguished Lecturer, November, 2000
- President, American Association for Pharmaceutical Scientists, 2001
- Research Achievement Award in the Pharmaceutical Sciences, American Pharmaceutical Association, 2001
- University of Southern California, School of Pharmacy, Distinguished Lecturer, 2001
- Medeval Distinguished Lecturer in the Pharmaceutical Sciences, 2001
- Honorary Doctorate Degree Royal Danish School of Pharmacy, 2002
- Takeru Higuchi Research Prize, American Pharmaceutical Association, 2003
- Smissman-Bristol-Myers Squibb Award, American Chemical Society, Division of Medicinal Chemistry, 2003
- University of Pittsburgh, School of Pharmacy, Distinguished Lecturer, 2003
- Doctor Honoris Causa (Honorary Doctorate Degree) Catholic University of Leuven, 2004
- Bristol-Myers Squibb Distinguished Lecturer University of Buffalo, State University of New York, 2004

Predoctoral and Postdoctoral Students and Visiting Scientists Trained by Ronald T. Borchardt

Trainee	Predoc/	Period	Present Employment
h	Postdoc		
harmaceutical Chemistr		1991-92	Scientist Taiche Pharmacoutical Co
Aikawa, K.	0		Scientist, Taisho Pharmaceutical Co.
Akimoto, KatsuyaVisi		1996-97	Scientist, Daiichi Pharmaceuticals
Ali, Mashood	Postdoc	1989-91	Assist. Prof., Aligaru Univ., India
Amsberry, Kent	Predoc	1984-89	Sr. Scientist, Quintile's, Inc.
Andersen, Rikke	Visiting Sci.	2001	Student, Royal Danish School of Pharmacy
Audus, Ken	Postdoc	1984-86	Professor & Chair, Univ. of Kansas
Augustijns, Patrick Vi		1992-93	Professor, Univ. of Leuven, Belgium
Bak, Annette	Visiting Sci.	1996-97, 1998-99Scientist,	, Amgen Corp.
Bartel, Ronnda	Postdoc	1986-89	Sr. Director, SRS Capital
Beck-Westermeyer, M		1996-00	Research Assoc., Covance
Berglund, Petter	Visiting Sci.	1998	Student, Royal Danish School of Pharmacy
Borcherding, D.	Postdoc	1986-88	Sr. Scientist, Aventis
Brazell, Celia	Postdoc	1984-86	Sr. Scientist, GlaxoSmithKline, England
Bross, Becky	Predoc	2003-	Present student
Brunt, Elsbeth	Predoc	1991-94	Administrator, FDA
Camenisch, Gian	Postdoc	1997-98	Sr. Scientist, Novartis, Switzerland
Chastain, Jim	Postdoc	1986-88	Director, Alcon Labs
Chen, Wei Qing	Postdoc	1999-02	Scientist, Pharmacopeia
Chikhale, P.	Postdoc	1991-94	Assist. Prof., Univ. of Maryland
Cools, Marina	Visiting Sci.	1988	Scientist, Jansen Pharmac. Co., Belgium
Eriksson, Andre	Visiting Sci.	2000	Student, Royal Danish School of Pharmacy
Fernando, A.	Postdoc	1991-92	Sr. Lecturer, University of Kelaniya, Sri Lanka
Friedrichson, Gerda	Visiting Sci.	1999-00	Scientist, Leo Pharmaceuticals, Denmark
Fuchs, Tarra	Postdoc	2003-	· · · · · · · · · · · · · · · · · · ·
Fukuta, M.		1990	Present student
	Visiting Sci.		Assoc. Res. Head, Takeda Pharm. Corp., Japan
Gangwar, S.	Postdoc	1992-96	Sr. Scientist, Corixa Pharmaceuticals
Gao, Jinnian	Predoc	1995-00	Scientist, Bristol-Myers Squibb
Garren, Julie	Predoc	1983-88	Sr. Scientist, Abbott Laboratories
Ghezzo, Elena	Visiting Sci.	1991	Research Associate, Univ. of Kansas
Ghosh, Anil	Postdoc	1983-86	Asst. Director, Indian Inst. of Chemical Biol., India
Goolcharran, Charlie		1994-99	Scientist, Regeneron Inc.
Gray, Ronda	Predoc	1988-92	Sr. Scientist, Johnson & Johnson Pharm. Co.
Guan, Xiangming	Postdoc	1991-92	Assoc. Prof., Univ. of South Dakota
Gudmundsson, Olafur	Predoc	1994-98	Scientist, Bristol-Myers Squibb
Hasobe, Masa.	Postdoc	1986-89	Assoc. Prof., Tokyo Univ., Japan
Head, Kevin	Predoc	2001-	Present student
Hidalgo, Ismael	Postdoc	1986-90	Scientific Director, Absorption Systems
Hillgren, Kathy	Predoc	1988-94	Scientist, Eli Lilly
Hori, Kazutoshi	Visiting Sci.	2000-01	Scientist, Shionogi & Co., Japan
Hu, Ming,	Postdoc	1988-90	Assoc. Prof., Washington State Univ.
Hu, Yongbo	Postdoc	1999-02	Scientist, Wyeth Laboratories
Huang, He	Postdoc	1995-96	Director, Abrika Pharmaceuticals
Hugger, Erin	Predoc	1997-01	Scientist, GlaxoSmithKline
Hui, Ouyang	Postdoc	1999-01, 2002-	Postdoctoral Fellow
Huskey, SE.	Postdoc	1983-85	
Imai, Teruko	Visiting Sci.	1998	Sr. Scientist, Merck, Sharp and Dohme
Ishii, Hiroaki	Visiting Sci.	1987-88	Professor, Kumamoto University
Kakarla, Ramesh Post			Director, Pharmacia, Inc., Japan
		1988-91	Sr. Res. Invest., Bristol-Myers Squibb
Kanerva, Harri	Visiting Sci.	1995	Sr. Scientist, Orion Pharma, Finland
Kato, Akira,	Visiting Sci.	1988, 1992-93	Sr. Scientist, Eisai Co., Japan
Kawamura, Y.	Visiting Sci.	1992-94	Scientist, Dojin Iyaku Kako Co., Japan
Kawase, M.,	Postdoc	1985-87	Assoc. Prof., Josai Univ., Japan
Keller, Brad	Postdoc	1983-85	Sr. Res. Scientist, Pfizer
Khossravi, Mehrnaz		1994-99	Scientist, Centecor
Kim, Dong Chool	Postdoc	1991-93	Assoc. Professor, Chungnam Natl. Univ., Korea
Kolli, Sudha	M.S.	1993-94	Research Associate, Akorn, Inc.
Knipp, Greg	Predoc	1992-9 7	Assist. Professor, Rutgers University
	a Lidia Postdoc	1996-98	Consultant
Kupczyk-Subotkowska	, Diam I obtable		Consultant
Lai, Mei	Predoc	1993-98	
			Scientist, Bristol-Myers Squibb

I: Dana	Dundas	1007.01	Colombial Dhamasaia
Li, Rong	Predoc	1997-01	Scientist, Pharmacia
Li, Shihong	Predoc	1991-95	Sr. Scientist, Pfizer
Liederer, Bianca	Predoc	2000-	Present student
Liu, Siming	Postdoc	1991-94	Postdoctoral Fellow, North Carolina State Univ.
Matuszewska, B.	Postdoc	1981-85	Sr. Res. Fellow, Merck, Sharp and Dohme
Miller, Donald	Postdoc	1991-93	Assoc. Professor, Univ. of Nebraska
Murase, Osamu	Visiting Sci.	1999	Scientist, Organon Pharmaceuticals, Japan
Nakagami, Hiroaki	Visiting Sci.	1992	Sr. Scientist, Daiichi Pharm. Co., Japan
Narayanan, Su.	Postdoc	1986-88	Sr. Scientist, Aventis
Nerurkar, Manoj	Predoc	1992-96	Sr. Scientist, Bristol-Myers Squibb
Ng, Lawrence	Postdoc	1991-94	Assist. Prof., University of Colorado
Nicolaou, Mike	Predoc	1990-96	Assoc. Director, Epimune
Nielsen, Lisbeth	Visiting Sci.	2001	Scientist, Lundbeck Pharmaceuticals, Denmark
Nigam, S. C.	Postdoc	1988-91	Scientist, ISP Fine Chemicals
Nimkar, Kalpana	Postdoc	1996-97	Consultant
Nonomura, M.	Postdoc	1990-91	Assoc. Res. Head, Takeda Pharm. Corp., Japan
Okumu, Franklin	Predoc	1992-96	Scientist, Optimer Pharmaceuticals
Oliyai, Cecilia	Predoc	1988-93	Sr. Scientist, Corixa Pharmaceuticals
Ostergaard, Jesper	Visiting Sci.	1999	Graduate Student, Royal Danish School of Pharm.
Owens, Heather	M.S.	2000-02	Pharmacy Residency
Paisley, Steven	Postdoc	1986-88	Principal Investigator, Pharmacia
Patel, Kamlesh	Predoc	1985-89	Sr. Scientist, GlaxoSmithKline
			·
Pauletti, Giovanni Pos		1993-97	Asst. Professor, Univ. of Cincinnati
Pryor, Celestia	Postdoc	1987-90	Assoc. Prof., Univ. of the Pacific
Raeissi, Shamsi	MS	1988-92	Scientist, Pfizer
Ranta, Veli Pekka Vis		1997-98	Graduate Student, Univ. of Kuopio, Finland
Salfer, Dorothee	Visiting Sci.	1999	Student, Marburg Univ., Germany
Schoneich, C.	Postdoc	1991-92	Assoc. Professor, Univ. of Kansas
Scriba, Gerhard	Postdoc	1985-88	Professor, University of Jena, GDR
Shah, Mandar	Predoc	1985-91	Sr. Scientist, Alcon Labs
Shah, Praful	Predoc	1985-90	Director, NaPro
Simmons, J.	Postdoc	1983-85	Administrator, FDA
Sinhababu, A.	Postdoc	1980-88	Director, Genentech
Smith, Kevin	Postdoc	1986-89	Manager, Cephalon Corp.
Sonderkaer, Susanne	Visiting Sci.	1999	Graduate Student, Royal Danish School of Pharm.
Song, Yuan	Postdoc	1998-2001	Scientist, Inhale Corp.
Sorensen, Mette	Visiting Sci.	1996	Graduate Student, Royal Danish School of Pharmacy
Steenberg, Betina	Visiting Sci.	1996	Graduate Student, Royal Danish School of Pharmacy
Stevenson, C.	Predoc	1988-92	Sr. Scientist, Inhale Corp.
Sudoh, Masao	Visiting Sci.	1995-96	Scientist, Ono Pharm. Co., Japan
Takakura, Yoshi	Visiting Sci.	1989-90	Professor, Kyoto Univ., Japan
Tamura, Kiyoshi	Visiting Sci.	1994-96	Sr. Scientist, Banyu Pharmaceuticals
Tang, Fuxing	Postdoc	2000-02	Scientist, Forest Laboratory
Thombre-Patel, U.	Postdoc	1982-84	Consultant
Toddywalla, V.S.	Visiting Sci.	1988-89	Sr. Scientist, Inst. Res. Reproduction, India
Trammel, Andy	Predoc	1985-90	Sr. Scientist, Quintile's Inc.
Turner, Greg	Postdoc	1987-88	Group Leader, Midwest Research Institute
vanBree, Joost	Visiting Sci.	1988	•
Votruba, I.	~	1987-88	Sr. Scientist, Novartis, Switzerland
•	Visiting Sci.		Sr. Scientist, Czech. Academy of Science
Wakankar, Adiyta Pre		2001-	Present student
Wang, Binghe	Postdoc	1992-93	Professor, Georgia State Univ.
Wang, Wen	Postdoc	1993-97	Physician
Wilson, Ashley	Predoc	1994-00	Scientist, Eli Lilly
Wolfe, Janet	Predoc	1985-92	Consultant
Xie, Minli	Predoc	1993-97	Sr. Scientist, DuPont Pharmaceuticals
Yang, Jerry	Predoc		Scientist, Pfizer
Yang, Xiaoda	Postdoc	1997-00	Professor, Peking Univ. Med. Ctr., China
Yeh, Jerry	Postdoc	1986-92	Sr. Scientist, Alza Corp.
Yike, Iwona	Postdoc	1983-85	Res. Asst. Prof., Case Western Res. Univ.
Yin, Daniel	Postdoc	1997-01	Scientist, Merck Sharp & Dohme
Yu, Qiang	Postdoc		Scientist, SynChem
•	Postdoc	1991-97	Managing Director, Diazyme Laboratories
Zhang, Jinsong	Postdoc	2001-2003	Res. Asst. Prof., Univ. of Kansas Medical Center

Molecular Sciences Department (formerly Biochemistry Department)
Ault-Riche, Dana Predoc 1989-94
Baranczyk-Kuzma, A. Visiting Sci. 1980-81 Founder and CEO, Pointilliste Prof., Warsaw Medical School, Poland

Bartel, Ronnda	Predoc	1979-84	Sr. Director, SRS Capital			
Bhatia, Pramila	MS	1974-76	Research Associate, Abbott Laboratories			
Cai, Sumin	Predoc	2004-	Present student			
Chen, Hu	Predoc	2004-	Present student			
Chen, Shiang Y.	Postdoc	1979-80	Sr. Scientist, Glaxo-Wellcome			
Cheng, Chao Fu	Predoc	1971-75	Research Associate, Cornell University			
Elrod, Philip	MS	1998-00	Research Associate, Pharmacia, Inc.			
Huber, Joan	Postdoc	1974-84	Consultant			
Huskey, Su-Er W.	Predoc	1975-79	Sr. Res. Fellow, Merck, Sharp and Dohme			
Lee, Younha	Predoc	1988-93	Postdoctoral Fellow, Glaxo-Wellcome			
Liang, Nina	Postdoc	1980-83	Sr. Scientist, IBM			
Liang, Sherrie	MS	1988-92	Research Assistant, Univ. of Calgary, Canada			
Olsen, Julie	Postdoc	1976-78	Professor, Wabush College			
Patel-Thombre, U.	Predoc	1978-82	Consultant			
Pugh, Charles	Predoc	1976-79	Scientific Writer, Consultant			
Ramakrishnan, V.	Predoc	1981-86	Sr. Scientist, Core Therapeutics			
Scharnhorst, D.	Postdoc	1979-80	Physician, Private practice			
Schasteen, C.	Predoc	1975-80	Director, Novus Corp.			
Thakker, D.	Predoc	1972-75	Ferguson Distinguished Prof., Univ. of North Carolina			
Thomas, P.	MS	1979-81	Professor, Univ. of Kansas			
Varia, Smita T.	Predoc	1978-83	Res. Asst. Professor, Rutgers University			
Wang, Meng Meng	Predoc	2001-	Present student			
Wu, Yih Shiong	Predoc	1972-76	Retired			
Yu, Xiao Hong	Predoc	1993-96	Patent Attorney, University of California-San Diego			
, , ,			, , , , , , , , , , , , , , , , , , ,			
Medicinal Chemistry Department						
Bartlett, Bill	MS	1986-89	Pharmacist			
Borcherding, D.	Predoc	1981-86	Sr. Scientist, Aventis			
Houston, Mike	Predoc	1978-83	Sr. Scientist, Quintile's			
Moorman, Allan	Predoc	1978-83	Executive Director, King Pharma			
Sheley, John	MS	1990-94	Chemist, Ricerca, Inc.			
Wolfe, Mike	Predoc	1984-90	Assoc. Professor, Harvard University			
•						

Current and Pending Support

Ronald T. Borchardt The University of Kansas, Lawrence, KS

ACTIVE

•GM-29332 (PI, R.T. Borchardt)

02/01/03 to 01/31/07

15% (PI)

\$220,000 (Year 30)

AdoHcy Hydrolase: Inhibitors as Antiparasitic Agents

This grant supports research aimed at elucidating the structure and mechanism of catalysis of S-adenosylhomocysteine hydrolase and designing and synthesizing potential inhibitors of the human and parasitic (Trypansoma and Leishmania) forms of this enzyme.

•GM-51633 (PI, R.T. Borchardt)

07/01/99 to 06/30/04

15% (PI)

NIH

\$170,576 (Year 8)

Transport Characteristics of Peptide Mimetics

This grant supports research aimed at elucidating how bioisosteres of the peptide bond affect the permeability of peptide mimetics through the intestinal mucosa and the blood-brain barrier and their clearance by the liver.

•DA-09315 (PI, R.T. Borchardt)

07/01/03 to 06/30/08

15% (PI)

NIDA

Cyclic Prodrugs of Opioid Peptide

This grant supports research aimed at preparing cyclic prodrugs of opioid peptides which could improve their permeability through the intestinal mucosa and the blood-brain barrier.

\$175,000 (Year 8)

•GM-54195 (PI, E. Topp)

08/01/00 to 07/31/04 \$170,000 (Year 5)

15% (Co-Invest)

Peptide Degradation in Polymer Matrices

This grant supports research aimed at elucidating the pathways by which peptide and protein drugs chemically degrade in polymeric delivery systems.

•GM-08359 (PI, C. R. Middaugh)

07/01/02 to 06/30/07

5% (Preceptor)

NIH

\$244,864 (Year 14)

Pharmaceutical Aspects of Biotechnology Training

This grant supports the training of pharmaceutical scientists to handle the development of products arising from biotechnology.

•CA-09242 (PI, J.F. Stobaugh) 04/01/00 to 03/31/05 2.5% (Preceptor)

NIH \$265,000 (Year 25)

Clinical Analysis of Anticancer Drugs-Pre and Postdoctoral Training Grant

This grant supports predoctoral and postdoctoral trainees in the Departments of Pharmaceutical Chemistry and Chemistry in the area of clinical analysis of anticancer drugs.

•GM069663 (PI, J. Aube) 09/15/03-09/14/08 4% (Collaborator)

NIH \$2,430,741 (Year 1)

Center of Excellence in Chemical Methodologies and Library Development.

This P50 grant is focused on the development of innovative combinatorial chemistry.

PENDING

• EB000253 (PI, E. Topp) 08/01/04-07/31/09 10% (Co-PI)

NIH \$250,000 (Year 6)

Peptide and Protein Degradation in Amorphous Solids

This competitive renewal application would support the investigation of the kinetics and mechanisms of peptide and protein degradation in amorphous solids.

Publications:

- 1. S. M. Kupchan, T. H. Yang, M. L. King and R. T. Borchardt, "Thalictrum Alkaloids, VIII. The Isolation, Structural Elucidation and Synthesis of Dehydrothalcarpine", J. Org. Chem., 33, 1052-1055 (1968).
- Ronald T. Borchardt, "A Stereochemical Approach to the Adrenergic System", Ph.D. Thesis, University of Kansas, 1970.
- 3. E. E. Smissman and R. T. Borchardt, "A Conformational Study of Catecholamine Receptor Sites. V. The Synthesis of dl-3-Amino-2-(3', 4'-dihydroxyphenyl)-trans-decalol Hydrochlorides", J. Med. Chem., 14, 377-382 (1971).
- 4. E. E. Smissman and R. T. Borchardt, "A Conformational Study of Catecholamine Receptor Sites. VI. The Synthesis of dl-3-Amino-2-(3', 4'-dihydroxyphenyl)-trans-decalin Hydrochlorides", J. Med. Chem., 14, 383-387 (1971).
- E. E. Smissman and R. T. Borchardt, "Conformational Study of Catecholamine Receptor Sites. VII. Syntheses of erythro- and threo-2-Amino-3-(3', 4'-dihydroxyphenyl)-butane Hydrochlorides", J. Med. Chem., 14, 701-707 (1971).
- E. E. Smissman, R. T. Borchardt and K. B. Schowen, "Conformational Aspects of Systems Related to Acetylcholine. IV. The Syntheses of the dl-2-Dimethylamino-trans-decalin Methiodides", J. Med. Chem., 15, 545-548 (1972).
- R. T. Borchardt and L. A. Cohen, "Stereopopulation Control. II. Rate Enhancement of Intramolecular Nucleophilic Displacement", J. Amer. Chem. Soc., 94, 9166-9174 (1972).
- 8. R. T. Borchardt and L. A. Cohen, "Stereopopulation Control. III. Facilitation of Intramolecular Conjugate Addition of the Carboxyl Group", J. Amer. Chem. Soc., 94, 9175-9182 (1972).
- 9. R. T. Borchardt, "Catechol-O-Methyltransferase. I. Kinetics of Tropolone Inhibition", J. Med. Chem., 16, 377-382 (1973).
- R. T. Borchardt, "Catechol-O-Methyltransferase. II. <u>In Vitro</u> Inhibition by Substituted 8-Hydroxyquinolines", *J. Med. Chem.*, 16, 382-387 (1973).
- R. T. Borchardt, "Catechol-O-Methyltransferase. III. Mechanism of Pyridoxal 5'-Phosphate Inhibition", J. Med. Chem., 16, 387-391 (1973).
- R. T. Borchardt, "Catechol-O-Methyltranferase. IV. <u>In Vitro</u> Inhibition by 3-Hydroxy-4-Pyridones and 3-Hydroxy-2-Pyridones", J. Med. Chem., 16, 581-583 (1973).
- R. T. Borchardt and D. Thakker, "Affinity Labeling of Catechol-O-Methyltransferase", Biochem. Biophys. Res. Commun., 54, 1233-1239 (1973).
- R. T. Borchardt and L. A. Cohen, "Stereopopulation Control. IV. Facilitation of Intramolecular Conjugate Addition of Solvated Hydroxyl Groups", J. Amer. Chem. Soc., 95, 8303-8313 (1973).
- R. T. Borchardt and L. A. Cohen, "Stereopopulation Control. V. Facilitation of Intramolecular Conjugate Addition of an Aldehyde Hydrate and Hemiacetal", J. Amer. Chem. Soc., 95, 8313-8319 (1973).
- R. T. Borchardt and L. A. Cohen, "Stereopopulation Control. VI. Conformational Selection of Alternative Oxidative Pathways", J. Amer. Chem. Soc., 95, 8319-8326 (1973).
- C. R. Creveling, R. T. Borchardt, and C. Isersky, "Immunological Characterization of Catechol-O-Methyltransferase", in <u>Frontiers in Catecholamine Research</u> (E. Usdin and S. H. Snyder, Eds.), Pergamon Press, New York, p. 117-119 (1973).
- R. T. Borchardt, "A Rapid Spectrophotometric Assay for Liver Catechol-O-Methyltransferase", Anal. Biochem., 58, 382-389 (1974).
- R. T. Borchardt, C. F. Cheng, P. H. Cooke and C. R. Creveling, "Purification and Properties of Microsomal Catechol-O-Methyltransferase", *Life Sciences*, 14, 1089-1100 (1974).
- R. T. Borchardt and P. E. Hanna, "Histamine-N-Methyltransferase: Inhibition and Potentiation by <u>trans</u> and <u>cis</u>-1, 5-Diphenyl-3-dimethyl-aminopyrrolidine", J. Med. Chem., 17, 471-473 (1974).
- R. T. Borchardt and Y. S. Wu, "Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases. I. Modification of the Amino Acid Portion of S-Adenosylhomocysteine", J. Med. Chem., 17, 862-868 (1974).
- 22. R. T. Borchardt, J. A. Huber and Y. S. Wu, "Potential Inhibitors of S-Adenosylmethionine-Dependent

- Methyltransferases. II. Modification of the Base Portion of S-Adenosylhomocysteine", J. Med. Chem., 17, 868-873 (1974).
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- R. T. Borchardt and D. R. Thakker, "Catechol-O-Methyltransferase. VI. Affinity Labeling with N-Haloacetyl-3,5-Dimethoxy-4-Hydroxyphenylalkylamines", J. Med. Chem., 18, 152-158 (1975).
- R. T. Borchardt and Y. S. Wu, "Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases. III. Modifications of the Sugar Portion of S-Adenosylmethionine", J. Med. Chem., 18, 300-304 (1975).
- R. T. Borchardt, C. F. Cheng and D. R. Thakker, "Purification of Catechol-O-Methyltransferases by Affinity Chromatography", Biochem. Biophys. Res. Commun., 63, 69-77 (1975).
- R. T. Borchardt, "Affinity Labeling of Catechol-O-Methyltransferase by the Oxidation Products of 6-Hydroxydopamine", Mol. Pharmacol., 11, 436-449 (1975).
- R. T. Borchardt, "Inhibition of Indoleethylamine-N-Methyltransferase by Analogs of S-Adenosylhomocysteine", Biochem. Pharmacol., 24, 1542-1544 (1975).
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- R. T. Borchardt and D. R. Thakker, "Affinity Labeling of Catechol-O-Methyltransferase by N-Haloacetyl Derivatives of 3,5-Dimethoxy-4-Hydroxyphenylethylamine and 3,4-Dimethoxy-5-Hydroxyphenylethylamine. Kinetics of Inactivation", Biochemistry, 14, 4543-4551 (1975).
- 33. E. E. Smissman, J. R. Reid, D. A. Walsh and R. T. Borchardt, "Synthesis and Biological Activity of 2- and 4-Substituted-6,7-Dihydroxy-1,2,3,4-Tetrahydroisoquinoline", J. Med. Chem., 19, 127-131 (1976).
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 Affinity Labeling with the Oxidation Products of 6-Aminodopamine", J. Med. Chem., 19, 30-37 (1976).
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- R. T. Borchardt, "Catechol-O-Methyltransferase: A Model to Study the Mechanism of 6-Hydroxydopamine Interaction with Proteins", in <u>Chemical Tools in Catecholamine Research (</u>G. Jonsson, T. Malmfors and C. Sachs, Eds.), North Holland Publishing Company, Amsterdam, p. 33 -40, 1975.
- 37. R. T. Borchardt, J. A. Huber and Y. S. Wu, "A Convenient Preparation of S-Adenosylhomocysteine and Related Compounds", J. Org. Chem., 41, 565-567 (1976).
- 38. R. T. Borchardt, D. R. Thakker, W. D. Warner, D. M. Mirth and J. N. Sane, "Catechol-O-Methyltransferase. 8. Structure-Activity Relationship for Inhibition by 8-Hydroxyquinoline", J. Med. Chem., 19, 558-560 (1976).
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- R. T. Borchardt, Y. S. Wu and J. A. Huber, "Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases. IV. Further Modifications of the Amino Acid and Base Portions of S-Adenosylhomocysteine", J. Med. Chem., 19, 1094-1099 (1976).
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- R. T. Borchardt, J. A. Huber, A. F. Wycpalek and Y. S. Wu, "Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases. VI. Structural Modifications of S-Adenosylmethionine", J. Med. Chem., 19, 1104 -1110 (1976).
- 44. R. T. Borchardt, D. R. Thakker and J. R. Reid, "Catechol-O-Methyltransferase. 9. Mechanism of Inactivation by 6-Hydroxydopamine", J. Med. Chem., 19, 1201-1209 (1976).
- R. T. Borchardt and D. R. Thakker, "Evidence for Sulfhydryl Groups at the Active Site of Catechol-O-Methyltransferase", Biochim. Biophys. Acta, 445, 598-609 (1976).
- R. T. Borchardt and D. R. Thakker, "Affinity Labeling of Catechol-O-Methyltransferase Using N-Haloacetyl Derivatives
 of 3,5-Dimethoxy-4-Hydroxyphenylethylamine and 3,4-Dimethoxy-5-Hydroxyphenylethylamine", in <u>Methods in
 Enzymology-Affinity Labeling (</u>W. B. Jocoby and M. Wilcheck, Eds.), Academic Press, New York, Vol. 46, p. 554-561,
 1977.
- 47. R. T. Borchardt, W. C. Vincek and G. L. Grunewald, "A Liquid Chromatographic Assay for Phenylethanolamine N-Methyltransferase", Anal. Biochem., 82, 149-151 (1977).
- 48. R. T. Borchardt, S. K. Burgess, J. R. Reid, Y. O. Liang and R. N. Adams, "Effects of 2- and/or 5-Methylated Analogs of 6-Hydroxydopamine of Noradrenergic and Dopaminergic Neurons", Mol. Pharmacol., 13, 805-818 (1977).
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- R. T. Borchardt, "Chemical Probes of the Active Site of Catechol-O-Methyltransferase", in <u>Biochemistry and Function of Monoamine Enzymes</u> (E. Usdin and N. Weiner, Eds.), Marcel Dekker, New York, p. 707-726, 1977.
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- 57. R. T. Borchardt, Y. S. Wu and B. S. Wu, "Mechanism of Inhibition of Pineal Hydroxyindole-O-Methyltransferase by Pyridoxal 5'-Phosphate", *Biochem. Pharmacol.*, 27, 120-122 (1978).
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- R. T. Borchardt, J. Olsen, L. Eiden, R. L. Schowen and C. O. Rutledge, "The Isolation and Characterization of the Methyl Acceptor Proteins from Adrenal Chromaffin Granules", Biochem. Biophys. Res. Commun., 83, 970-976 (1978).
- 62. R. T. Borchardt, J. A. Huber and Y. S. Wu, "An Improved Synthesis of S-Adenosylhomocysteine", in <u>Nucleic Acid</u>
 <u>Chemistry; Improved and New Synthetic Procedures: Methods and Techniques (</u>L. B. Townsend and R. S. Tipson, Eds.), Wiley-Interscience, New York, Part II, p. 541-545, 1978.
- 63. R. T. Borchardt, M. F. Hegazi, S. Osaki and R. L. Schowen, "S-Adenosyl-L-Methionine-CD3 and S-Adenosyl-L-

- Methionine-¹³CH₃", in <u>Nucleic Acid Chemistry; Improved and New Synthetic Procedures: Methods and Techniques</u> (L. B. Townsend and R. S. Tipson, Eds.), Wiley-Interscience, New York, Part II, p. 889-894, 1978.
- R. T. Borchardt, "The Mechanism of Alkaline Hydrolysis of S-Adenosyl-L-Methionine and Related Sulfonium Nucleosides", J. Amer. Chem. Soc., 101, 458-463 (1979).
- 65. R. T. Borchardt, Y. S. Wu and B. S. Wu, "Affininty Labeling of Histamine-N-Methyltransferase by 2',3'-Dialdehyde Derivatives of S-Adenosylhomocysteine and S-Adenosylmethionine. Kinetics of Inactivation", *Biochemistry*, 17, 4145-4153 (1978).
- R. T. Borchardt, Y. S. Wu and B. S. Wu, "Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases.
 Role of the Ribosyl Moiety in Enzymatic Binding of S-Adenosylhomocysteine and S-Adenosylmethionine", J. Med. Chem., 21, 1307-1310 (1978).
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Patents

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Editor

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- 8. V. Stella, M. Hageman, R. Oliyai, J. Tilley, H. Maag and R. T. Borchardt (Eds.), "Prodrugs: Challenges and Rewards", in the series entitled, "Biotechnology: Pharmaceutical Aspects" (R. T. Borchardt and C. R. Middaugh, Series Editors), AAPS Press, Arlington, VA, in preparation.
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Series Editor

A) Pharmaceutical Biotechnology, Plenum Press (1992-2002)

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- L. Sanders and W. Hendren (Eds.), "Protein Delivery: Physical Systems", Vol. 10 in the series entitled, "Pharmaceutical Biotechnology" (R. T. Borchardt, Series Editor), Plenum Press, New York, NY, 1997.
- 11. R. T. Borchardt, R. M. Freidinger, T. Sawyer and P. Smith (Eds.), "Integration of Pharmaceutical Discovery and Development: Case Histories", Vol. 11 in the series entitled, "Pharmaceutical Biotechnology" (R. T. Borchardt, Series Editor), Plenum Press, New York, NY, 1998.
- G. Amidon and W. Sadee (Eds.), "Membrane Transporters as Drug Targets", Vol. 12 in the series entitled, "Pharmaceutical Biotechnology" (R. T. Borchardt, Series Editor), Kluwer Academic/Plenum Press, New York, NY, 1999.
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B) Biotechnology: Pharmaceutical Aspects (2002-present)

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- 2. R. T. Borchardt, E. H. Kerns, C. A. Lipinski, D. R. Thakker and B. Wang (Eds.), "Pharmaceutical Profiling in Drug Discovery for Lead Selection", Vol. 2 in the series entitled, "Biotechnology: Pharmaceutical Aspects" (R. T. Borchardt and C. R. Middaugh, Series Editors), AAPS Press, Arlington, VA, in production.
- 3. W. Jiskoot and D. Crommelin (Eds.), "Methods for Structural Analysis of Protein Pharmaceuticals", Vol. 3 in the series entitled, "Biotechnology: Pharmaceutical Aspects" (R. T. Borchardt and C. R. Middaugh, Series Editors), AAPS Press, Arlington, VA, in preparation.
- 4. V. Stella, M. Hageman, R. Oliyai, J. Tilley, H. Maag and R. T. Borchardt (Eds.), "Prodrugs: Challenges and Rewards Part I", Vol. 4 in the series entitled, "Biotechnology: Pharmaceutical Aspects" (R. T. Borchardt and C. R. Middaugh, Series Editors), AAPS Press, Arlington, VA, in preparation.
- 5. V. Stella, M. Hageman, R. Oliyai, J. Tilley, H. Maag and R. T. Borchardt (Eds.), "Prodrugs: Challenges and Rewards Part II", Vol. 5 in the series entitled, "Biotechnology: Pharmaceutical Aspects" (R. T. Borchardt and C. R. Middaugh, Series Editors), AAPS Press, Arlington, VA, in preparation.
- 6. R. T. Borchardt, E. H. Kerns, D. R. Thakker, S. Sittampalam, M. J. Hageman, J. L. Stevens (Eds), "Optmization of the Drug-like Properties of Leads", Vol. 6 in the series entitled "Biotechnology: Pharmaceutical Aspects" (R. T. Borchardt and C. R. Middaugh, Series Editors), AAPS Press, Arlington, VA, in preparation.

Short Courses

A) Professional Association Short Courses

- Organized and participated in the AAPS-sponsored short course entitled, "Cell Lines and Tissue Culture in Pharmaceutical Research and Development", San Diego, CA, November, 1994.
- Organized and participated in the AAPS/EUFEPS-sponsored short course entitled, "Cell Lines and Tissue Culture in Pharmaceutical Research and Development", Edinburgh, Scotland, September, 1996.
- 3. Organized and participated in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal *In Vivo* Activity After Oral Administration", Princeton, NJ, July, 1997.
- 4. Organized and participated in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal In Vivo Activity After Oral Administration", Princeton, NJ, July, 1998.
- Participated in AAPS-sponsored short course entitled, "Applications of Cell Culture Systems in Academic and Industrial Pharmaceutical Research", Arlington, VA, August, 1998.
- 6. Co-organized and participated in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal Blood-Brain Barrier Permeability", Princeton, NJ, July, 1999.
- 7. Organized and participated in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal *In Vivo* Activity After Oral Administration", Princeton, NJ, June, 2000.
- 8. Participant in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal Blood-Brain Barrier Permeability", Princeton, NJ, June, 2000.
- Organized and participated in the Drew University-sponsored short course entitled, "Designing Drugs With Optimal In Vivo Activity After Oral Administration", Princeton, NJ, June, 2001.
- Organizer and participant in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal In vivo Activity After Oral Administration", Princeton, NJ, June, 2002.
- 11. Participated in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal Blood Brain Barrier Permeabilty", Princeton, NJ, June, 2002.
- Organizer and participant in the Drew University-sponsored short course entitled, "Designing Drugs with Optimal In Vivo Activity After Oral Administration", Princeton, NJ, June, 2003.
- Organizer and participant in the Drew University-sponsored short course entitled "Designing Drugs with Optimal In Vivo Activity After Oral Administration", Princeton, NJ, June, 2004.

B) On-site Short Courses

- Organizer and participant in a short course entitled, "Designing Drugs with Optimal In Vivo Activity After Oral Admiinistration", which was presented at the following pharmaceutical/biotechonlogy companies:
 - Chiron Corporation, December, 2000
 - Guilford Pharmaceuticals, April, 2001
 - Roche Bioscience (Palo Alto, CA), May, 2001
 - Eli Lilly Corporation, November, 2001
 - Albany Molecular Research Institute, November, 2001
 - 3D Pharmaceuticals, January, 2002
 - Pfizer Corporation (Ann Arbor, MI), January, 2002
 - Gilead Corporation, February, 2002
 - Pfizer (LaJolla, CA), February, 2002
 - Aventis, April, 2002
 - Roche (Nutley, NJ), April, 2002
 - Bristol-Myers Squibb, April, 2002
 - Serono (Geneva), July, 2002
 - Aventis (Frankfurt), July, 2002
 - Genomics Institute of the Novartis Research Foundation (LaJolla, CA), June, 2003
 - Quorex/Biota/Celgene (San Diego, CA), June, 2003
 - Millennium Pharmaceuticals (Cambridge, MA), June, 2004
 - AstraZeneca Pharmaceuticals (Waltham, MA), June, 2004

- Participant in a short course entitled, "Designing Drugs with Optimal Blood Brain Barrier Permeabilty" which was presented at the following pharmaceutical/biotechnology companies:

 Albany Molecular Research Institute, April, 2001

 Sepracor, September, 2002

 Eli Lilly Corporation, March, 2003 2.

Abstracts

- R. T. Borchardt. Kinetics of Tropolone Inhibition of Catechol-O-Methyltransferase. Midwest Regional Meeting, American Chemical Society, October, 1972.
- 2. R. T. Borchardt. Inhibition of Catechol-O-Methyltransferase by 8-Hydroxyquinolone. Midwest Regional Meeting, American Chemical Society, October, 1972.
- R. T. Borchardt. Mechanism of Pyridoxal 5'-Phosphate Inhibition of Catechol-O-Methyltransferase. West Central States Biochemistry Meeting, October, 1972.
- 4. R. T. Borchardt, J. A. Huber and Y. S. Wu. The Specificity of the S-Adenosylhomocysteine Binding Sites of Various Methyltransferases. Symposim on the Biological Role of S-Adenosylmethionine in Methyl Transfer and Polyamine Biosynthesis, Gif-sur-Yvette, France, June, 1973.
- R. T. Borchardt and D. Thakker. Affinity Labeling of Catechol-O-Methyltransferase. Midwest Regional Meeting, American Chemical Society, October, 1973.
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- R. T. Borchardt, J. A. Huber and Y. S. Wu. The Inhibition of Biological Transmethylation Reactions by Analogs of S-Adenosylhomocysteine. Midwest Regional Meeting, American Chemical Society, October, 1973.
- R. T. Borchardt. A Rapid Spectrophotometric Assay for Catechol-O-Methyltransferase. Midwest Regional Meeting, American Chemical Society, October, 1973.
- R. T. Borchardt. Synthesis and Biological Activity of Analogs of S-Adenosylhomocysteine as Inhibitors of Methyltransferases. Symposium on the Biochemistry of S-Adenosylmethionine, Rome, Italy, May, 1974.
- R. T. Borchardt and D. Thakker. Purification of Catechol-O-Methyltransferase by Affinity Chromatography. Midwest Regional Meeting, American Chemical Society, November, 1974.
- 11. R. T. Borchardt and D. Thakker. Affinity Labeling of Catechol-O-Methyltransferase. Midwest Regional Meeting, American Chemical Society, November, 1974.
- R. T. Borchardt. Irreversible Inhibition of Catechol-O-Methyltransferase by Various Polyphenolic Compounds. Midwest Regional Meeting, American Chemical Society, November, 1974.
- 13. R. T. Borchardt and Y. S. Wu. Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases. Modifications of the Ribose Portion of S-Adenosylhomocysteine. Midwest Regional Meeting, American Chemical Society, November, 1974.
- M. F. Hegazi, R. T. Borchardt and R. L. Schowen. Toward a Mechanism of COMT Action. Midwest Regional Meeting, American Chemical Society, November, 1974.
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- R. T. Borchardt. Catechol-O-Methyltransferase: A Model to Study the Mechanism of 6-Hydroxydopamine Interaction with Proteins. Symposium on Chemical Tools in Catecholamine Research. Goteburg, Sweden, July, 1975.
- 17. R. T. Borchardt and D. R. Thakker. Affinity Labeling of Catechol-O-Methyltransferase. Sixth International Congress of Pharmacology, Helsinki, Finland, July, 1975.
- R. T. Borchardt. New Approaches to Controlling the Activity of Phenylethanolamine-N-Methyltransferase in Stress.
 Symposium on Catecholamines and Stress, Bratislava, Czechoslovakia, July, 1975.
- R. T. Borchardt and D. R. Thakker. Probing the Active Site of Catechol-O-Methyltransferase. Symposium on Selected Topics of Interest to the Medicinal Chemist. American Chemical Society Meetings, Chicago, IL, August, 1975.
- R. T. Borchardt, E. E. Smissman, D. Nerland and J. R. Reid. The Mechanism of 6-Aminodopamine Inactivation of Catechol-O-Methyltransferase. Midwest Regional Meeting, American Chemical Society, November, 1975.
- R. T. Borchardt and D. R. Thakker. Kinetics of N-Ethylmaleimide Inactivation of Catechol-O-Methyltransferase. Midwest Regional Meeting, American Chemical Society, November, 1975.

- R. T. Borchardt, J. A. Huber and Y. S. Wu. Potential Inhibitors of S-Adenosylmethionine-Dependent Methyltransferases. Analogs of S-Adenosylmethionine. Midwest Regional Meeting, American Chemical Society, November, 1975.
- R. T. Borchardt, J. A. Huber and Y. S. Wu. A Convenient Preparation of S-Adenosylhomocysteine and Related Compounds. Midwest Regional Meeting, American Chemical Society, November, 1975.
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- R. T. Borchardt and C. F. Cheng. Purification of Rat Heart and Brain Catechol-O-Methyltransferase by Affinity Chromatography. Fed. Proc., 35 (Abst. #672) 1976.
- R. T. Borchardt, S. K. Burgess and J. R. Reid. Synthesis and Biological Activity of 2- and/or 5-Methylated Analogs of 6-Hydroxydopamine. Midwest Regional Meeting, American Chemical Society, October, 1976.
- R. T. Borchardt, C. Schasteen and S. E. Wu. Inhibition of Phenol-Sulfotransferase by Adenosine 3',5'-Diphosphate and Related Nucleotides. Midwest Regional Meeting, American Chemical Society, October, 1976.
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- R. T. Borchardt, S. K. Burgess, J. R. Reid, Y. O. Liang and R. N. Adams. Effects of 2- and/or 5-Methylated Analogs of 6-Hydroxydopamine on Noradrenergic and Dopaminergic Neurons. Fed. Proc., 36 (Abst. #3570), 1977.
- R. T. Borchardt, G. L. Grunewald, C. S. Aldrich and W. C. Vincek. Aromatic Analogs of Phenylethanolamine (PEA) as Substrates and Inhibitors of Phenylethanolamine-N-Methyltransferase (PNMT), American Chemical Society Meeting, March, 1977.
- C.S.G. Pugh, R. T. Borchardt and H. O. Stone. Inhibition of Newcastle Disease Virion: m-RNA (guanine-7-)methyltransferase by Analogs of S-Adenosylhomocysteine. American Chemical Society for Microbiology Meeting,
 May, 1977.
- R. T. Borchardt, Y. S. Wu and B. S. Wu. S-Adenosyl-L-homocysteine Dialdehyde: An Affinity Labelling Reagent for Histamine-N-Methyltransferase, Midwest Regional Meeting, American Chemical Society, November, 1977.
- R. T. Borchardt and C. S. Schasteen. Phenol-Sulfotransferase Inactivation by 2,3-Butanedione and Phenylgloxal: Evidence for an Active Site Arginyl Residue. Midwest Regional Meeting, American Chemical Society, November, 1977.
- R. T. Borchardt, Y. S. Wu and B. S. Wu. Affinity Labeling of Histamine-N-Methyltransferase by 2',3'-Dialdehyde Analogs of S-Adenosylmethionine and S-Adenosylhomocysteine. Fed. Proc., 37 (Abst. #1322) 1978.
- R. T. Borchardt. Approaches to the Design of Inhibitors of SAM-Dependent Methyltransferases. Central and Great Lakes Regional Meeting of the American Chemical Society, Symposium on Methyl Group Transfer Reaction, Indianapolis, IN, May, 1978.
- R. T. Borchardt, J. Olsen, L. Eiden, R. L. Schowen and C. Rutledge. Isolation and Characterization of the Methyl Acceptor Protein (MAP) from Adrenal Chromaffin Granules, Fourth International Catecholamine Symposim, Monterey, CA, Sept., 1978.
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- 389. J. Yang, K. C. Bastian, R. D. Moore, A. Bak, J. F. Stobaugh and R. T. Borchardt, "A Comparison of HPLC with Fluorescence Detection and LC/MS/MS for Quantitative Analysis of a Model Opioid Peptide and Its Cyclic Prodrug in Plasma", Millennial World Congress of Pharmaceutical Sciences, San Francisco, CA, April, 2000.
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- 397. R. T. Borchardt, "How Structure Influences the Cell Permeation of Peptides and Peptidemimetics", Millennial World Congress of Pharmaceutical Sciences, San Francisco, CA, April, 2000.
- R. T. Borchardt, "Biological Models to Assess Drug Bioavailability", Symposium entitled "Lipophilicity in Drug Disposition", Lausanne, Switzerland, March, 2000.
- E. D. Hugger, B. L. Novak and R. T. Borchardt, "Effect of Lipidic Excipents on Efflux Transporters in the Intestinal Mucosa", British Pharmaceutical Conference, Birmingham, England, Journal of Pharmacy and Pharmacology, 52, 192 (2000)
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- 423. S. Winslow, Q. Yu, T. Siahaan, R. T. Borchardt and E. M. Topp, "Synthesis of Model Cyclic β-Turn Peptides and Their Linear Analogs", AAPSPharmSci, 4 (Abst. M2336), 2001.
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- 430. F. Tang and R. T. Borchardt, "Do Rhodamine 123 and Hoechst 3342 Bind to the Same or Different Sites on P-Glycoprotein?", AAPSPharmSci, 5 (Abst. T2101), 2002.
- 431. W. Chen, J. Z. Yang, A. Bak, H. Ouyang and R. T. Borchardt, "Evaluation of the Intestinal Permeation Characteristics of a Model Opioid Peptide (DADLE) and Its Cyclic Prodrugs Using an *In Situ* Perfused Rat Ileum Model", AAPSPharmSci, 5 (Abst. R6139), 2002.
- 432. S. L. Winslow, Q. Yu, R. T. Borchardt, T. Siahaan and E. Topp, "Synthesis and Deamidation of Model β-Turn Peptides in the Solution and Solid States", AAPSPharmSci, 5 (Abst. T2093), 2002.
- 433. J. Ji., C. Schöneich, R. T. Borchardt and E. M. Topp, "Glutathone Disulfide Photolytic Degradation Produces an Aldehyde", AAPSPharmSci, 5 (Abst. T2127), 2002.
- 434. M. L. Houchin, R. T. Borchardt and E. M. Topp, "Effect of PLGA Film Incorporation on Peptide Deamidation", AAPS PharmSci, 5 (Abst. T2101), 2002.
- 435. R. T. Borchardt, "Educational and Communication Issues Associated with Integrating and Applying Drug-like Data in Drug Discovery", AAPS Workshop entitled, "Pharmaceutical Profiling in Drug Discovery for Lead Selection", Whippany, NJ, May, 2003.
- 436. R. T. Borchardt, "Scientific, Educational and Communication Issues Related to Candidate Selection", 45th Annual Land O'Lakes Conference entitled, "Rational Drug Product Design", Merrimac, WI, June, 2003.
- H. Ouyang and R. T. Borchardt, "Characterization of Breast Cancer Resistant Protein (MXR) in Cell Culture Models using Bi-directional Transport Assays", AAPSPharmSci, 6 (Abst. T2151), 2003.
- 438. B. Li, M. O'Meara, R. L. Schowen, E. M. Topp and R. T. Borchardt, "The Effects of Sucrose and Mannitol on the Rate of Deamidation of Asparagine Residues in Model Peptides in the Solid State", AAPSPharmSci, 6 (Abst. T3127), 2003.
- 439. B. Li, R. L. Schowen, E. M. Topp and R. T. Borchardt, "The Effects of the Residue on the N-Terminal Side of an Asparagine Residue on Its Rate of Deamidation in the Solid State", AAPSPharmSci, 6 (Abst. T3125), 2003.
- 440. B. Li, R. L. Schowen, E. M. Topp and R. T. Borchardt, "The Effects of a Carboxylate Side Chain on the C-Terminal Side of an Asparagine Residue on Its Rate of Deamidation", *AAPSPharmSci*, 6 (Abst. T3126), 2003.
- S. L. Winslow, D. S. Reddy, R. T. Borchardt and E. M. Topp, "Characterization and Deamidation of Model Cyclic β-Turn Peptides and Their Linear Analogs in Solution and the Solid State", Colorado Protein Stability Conference, Breckenridge, CO, July, 2003.
- M. L. Houchin, R. T. Borchardt and E. M. Topp, "Peptide Degradation and Recovery in PLGA Films", AAPSPharmSci, 6 (Abst. T2069), 2003.
- S. L. Winslow, D. S. Reddy, R. T. Borchardt and E. M. Topp, "Characterization and Deamidation of Model Cyclic β-Turn Peptides and Their Linear Analogs", AAPSPharmSci, 6 (Abst. T2107), 2003.
- 444. J. Ji, C. Schöneich, R. T. Borchardt and E. M. Topp, "Products of Glutathione Disulfide Photolytic Degradation in Solution", AAPSPharmSci, 6 (Abst. T3120), 2003.
- A. M. D'Souza, R. T. Borchardt, R. L. Schowen, J. S. Salsbury, E. J. Munson and E. M. Topp, "Polymer-Peptide Conjugates", AAPSPharmSci., 6 (Abst. M1272), 2003.
- 446. C. E. Stotz, D. Vander Velde, R. T. Borchardt and E. M. Topp, "Deamidation Rates Within β-Turn-containing

INVITED RESEARCH PRESENTATIONS

A. National or International Meetings

- "The Specificity of the S-Adenosylhomocysteine Binding Sites of Various Methyltransferases", Symposium on the Biological Role of S-Adenosylmethionine in Methyl Transfer and Polyamine Biosynthesis, Gif-sur-Yvette, France, June, 1973.
- "Synthesis and Biological Activity of Analogs of S-Adenosylhomocysteine as Inhibitors of Methyltransferases", Symposim on the Biochemistry of S-Adenosylmethionine, Rome, Italy, May, 1974.
- "Catechol-O-Methyltransferase: A Model to Study the Mechanism of 6-Hydroxydopamine Interaction with Proteins", Symposium on Chemical Tools in Catecholamine Research, Goteburg, Sweden, July, 1975.
- 4. "New Approaches to Controlling the Activity of Phenylethanolamine-N-Methyltransferase in Stress", Symposium on Catecholamines and Stress, Bratislava, Czechoslovakia, July, 1975.
- "Probing the Active Site of Catechol-O-Methyltransferase", Symposium on Selected Topics of Interest to the Medicinal Chemists, American Chemical Society Meeting, Chicago, Illinois, August, 1975.
- "Chemical Probes of the Active Site of Catechol-O-Methyltransferase", Symposium on Biochemistry and Function of Monoamine Enzymes, Steamboat Springs, Colorado, March, 1977.
- "Approaches to the Design of Inhibitors of SAM-Dependent Methyltransferases", Symposium on Methyl Transfer Reactions, Regional American Chemical Society Meeting, Indianapolis, Indiana, May, 1978.
- 8. "Isolation and Characterization of the Methyl Acceptor Protein from Adrenal Chromaffin Granules", 4th International Catecholamine Symposium, Monterey, California, September, 1978.
- "Approaches to the Design of Inhibitors of SAM-Dependent Methyltransferases", International Conference on Transmethylation, Bethesda, Maryland, October, 1978.
- "Biological Transmethylation Reactions", Symposium on Transmethylations at the ASBC Meeting, New Orleans, Louisiana, June, 1980.
- "Phenol Sulfotransferase: Purification and Characterization of the Rat Liver, Kidney and Brain Enzymes", Symposium
 on Phenol Sulfotransferase at the American College of Neuropsychopharmacology Annual Meeting, San Juan, Puerto
 Rico, December, 1980.
- "5-Substituted-3-Hydroxy-4-Methoxybenzaldehydes and Benzoic Acids as Inhibitors of Catechol-O-Methyltransferase", Conference on Monoamine Enzymes, Airlie House, Warrenton, Virginia, March, 1981.
- "Recent Studies on Inhibitors of Biological Transmethylation Reactions", Sato Award Presentation, Annual Meeting of the Pharmaceutical Society of Japan, Kumamoto City, Japan, April, 1981.
- 14. "Phenol Sulfotransferase: Purification and Characterization of a Rat Liver Enzyme", Workshop on Sulfate Metabolism and Sulfate Conjugation, Noordwijkerhout, The Netherlands, September, 1981.
- "Inhibitors of Biological Transmethylation Reaction", International Conference on Transmethylation, Lake of the Ozarks, October, 1981.
- 16. "Role of Central Epinephrine Neurons in Regulation of Serum Corticosterone Levels", Third Symposium on Catecholamines and Other Neurotransmitters in Stress, Smolenice Castle, Czechoslovakia, June, 1983.
- 17. "Role of Central Epinephrine Neurons in the Regulation of Serum Prolactin and Luteinizing Hormone Release in Female Rats" 5th International Catecholamine Symposim, Goteberg, Sweden, June, 1983.
- "Transport and Metabolism as Barriers to Macromolecular Drug Delivery", Academy of Pharmaceutical Sciences Meeting, Miami, Florida, November, 1983.
- 19. "In Vitro Biological Methods for Assessment of Oral Absorption", Land O'Lakes Conference, June, 1984.

- "S-Adenosylmethionine-Dependent Transmethylation of Histamine: Purification and Partial Characterization of Guinea
 Pig Brain and Rat Kidney Histamine N-Methyltransferase", Frontiers in Histamine Research: An International
 Symposium, Jouy-En-Josas, France, July, 1984.
- "Endogenous Macromolecules as Potential Targets for Site Directed Drug Delivery", Academy of Pharmaceutical Sciences Annual Meeting, Philadelphia, PA, Nov., 1984.
- "S-Adenosyl-L-homocysteine Hydrolase: A Potential Target for Drug Design", International Symposium entitled, "The Biochemistry of S-Adenosylmethionine as a Basis for Drug Design", Bergen, Norway, July, 1985.
- "Intestinal Epithelium and Vascular Endothelium as Barriers to Peptide and Protein Delivery", Chicagoland Pharmaceutical Discussion Group, January, 1986.
- 24. "Transport and Metabolism as Barriers to Absorption of Peptides and Proteins", Land O'Lakes Conference, June, 1986.
- 25. "Bovine Brain Microvessel Endothelial Cell Monolayers as a Model System for the Blood Brain Barrier", New York Academy of Science Symposium entitled, "Controlled Delivery of Drugs: Barriers, Technologies and Therapeutic Approaches", New York, January, 1987.
- 26. "Therapeutic Aspects of rDNA Proteins An Overview", symposium entitled, "r-DNA-Derived Proteins: Toxicologic Considerations", Society of Toxicology, Washington, DC, February, 1987.
- 27. "Viral Requiring Methylations as a Target for the Design of Antiviral Agents", NATO Advanced Study Institute: Antiviral Drug Development: A Multidisciplinary Approach", Il Ciocco, Italy, May, 1987.
- "Endothelial Cells of the Vasculature: A Significant Barrier to Effective Drug Delivery", Controlled Release Society, Inc. Meeting, Toronto, Canada, August, 1987.
- 29. "The Use of Isolated Epithelial and Cultured Endothelial Cells in the Design of Novel Drug Delivery Systems", Xth International Congress of Pharmacology, Sydney, Australia, August, 1987.
- "Transport Barriers in the Absorption of Peptide Drugs", 47th International Congress of Pharmaceutical Sciences of F.I.P., Amsterdam, The Netherlands, September, 1987.
- "Barriers to Absorption of Peptides", Disposition and Delivery of Peptide Drugs-International F.I.P. Satellite Symposium, Leiden, The Netherlands, September, 1987.
- 32. "S-Adenosylhomocysteine Hydrolase as a Potential Target for the Design of Antiviral Agents", Symposium entitled, "Enzyme Inhibition". 22nd Midwest Regional ACS Meeting, Wichita, KS, November, 1987.
- 33. "Protein Transport Across Cultured Brain Endothelial Cells", Symposium entitled, "Biological Transport Mechanisms as a Basis for Rational Drug Delivery", Fetzer Center, Kalamazoo, Michigan, November, 1987.
- 34. "Cultured Bovine Brain Microvessel Endothelial Cells: A Model System Useful in Studying the Transport and Metabolism of Peptides and Proteins Across the Blood Brain Barrier", International Conference on Pharmaceutical Sciences and Clinical Pharmacology, Jerusalem, Israel, June, 1988.
- 35. "Epithelial and Endothelial Barriers to the Effective Delivery of Proteins", Symposium entitled, "The Biology and Pharmacology of Hemopoietic Growth Factors", Newport, Rhode Island, June, 1988.
- 36. "Cultured Bovine Brain Capillary Endothelial Cells: A Model System for Blood-Brain Barrier Transport and Metabolism", 4th Japanese-American Conference on Pharmacokinetics and Biopharmaceutics, San Francisco, California, July, 1988.
- 37. "Elucidation of the Mechanism by Which Neplanocin A and 9-(Trans-2'-Trans-3'-Dihydroxycyclopent-4'-enyl)-Adenine Inactivate S-Adenosylhomocysteine Hydrolase", 8th International Round Table on Nucleosides and Nucleotides, Pensacola, Florida, October, 1988.
- 38. "Cultured Endothelial Cells: An In Vitro Model System for Studying Protein Transport and Metabolism". The Second Annual University of California-San Francisco Biotechnology Symposium, San Francisco, California, October, 1988.
- 39. "The Application of Cell Culture Models to Study Drug Transport Processes: An Overview". Symposium entitled, "Cell Culture as a Tool to Study Drug Transport Processes", American Association of Pharmaceutical Scientists Meeting, Orlando, Florida, November, 1988.
- 40. "Endothelial Cells of the Brain Vasculature: A Significant Barrier to CNS Drug Delivery". Frontiers of the Life Sciences Symposium, 1989 AAAS Annual Meeting, San Francisco, California, January, 1989.

- "Cultured Brain Microvessel Endothelial Cells: An <u>In Vitro</u> Model System to Evaluate Strategies for Drug Targeting to the Brain", BioScience 89, Malmo, Sweden, April, 1989.
- 42. "S-Adenosylhomocysteine Hydrolase: A Target for the Design of Antiviral Agents", Gordon Conference on Purines, Pyrimidines and Related Compounds, Salve Regina College, Newport, Rhode Island, July, 1989.
- 43. "The Use of Cultured Epithelial and Endothelial Cells to Study Drug Transport and Metabolism", Drug Delivery Systems Conference, Tokyo, Japan, July, 1989.
- 44. "Deamidation: A Major Pathway for Chemical Degradation of Proteins and Peptides", The Academy of Pharmaceutical Science and Technology Conference, Shirakaabako, Japan, July, 1989.
- 45. "Pharmaceutical Applications of Cell Culture: An Overview", NATO Advanced Research Workshop on Drug Transport in Cell Culture, Bandol, France, September, 1989.
- 46. "Development of <u>In Vitro</u> Blood-Brain Barrier Model Systems for Studying Drug Transport", The Preuss Foundation Seminar entitled, "The Role of the Blood-Brain Barrier in the Therapy of Brain Tumors", Scottsdale, Arizona, November, 1989.
- 47. "The Blood-Brain Barrier in Culture", The King's College Symposium entitled, "The Capillary Endothelium of the Brain", London, England, December, 1989.
- 48. "Rational Design of Antiviral Drugs", Indian Pharmaceutical Congress, Bombay, India, December, 1989.
- 49. "Biological Approaches to Rational Drug Delivery", Indian Pharmaceutical Congress, Bombay, India, December, 1989.
- 50. "In Vitro Models of the Blood Brain Barrier", Annual Meeting of the American College of Neuropyschopharmacology, Maui, Hawaii, December, 1989.
- 51. "Cultured Bovine Brain Microvessel Endothelial Cells: An In Vitro Model System to Study the Blood-Brain Barrier Permeability of Peptides and Proteins", AAPS Western Regional Meeting, Reno, Nevada, February, 1990.
- 52. "Assessment of Transport Barriers Using Cell and Tissue Culture Systems", 9th annual Update Conference in Pharmaceutics entitled, "A Critical Evaluation of Future Drug Forms - Drugs for the 21st Century", Madison, Wisconsin, April, 1990.
- 53. "Inhibitors of S-Adenosylhomocysteine Hydrolase: A Target for the Design of Antiviral Agents", 3rd International Conference on Antiviral Research, Brussels, Belgium, April, 1990.
- 54. "S-Adenosylhomocysteine Hydrolase: A Target for the Design of Antiviral Agents", 31st Annual Medicinal Chemistry Symposium, State University of New York at Buffalo, NY, June, 1990.
- 55. "Protein Transport Through Cultured Brain Microvessel Endothelial Cells, A Model of the Blood Brain Barrier", XIth International Congress of Pharmacology, Amsterdam, The Netherlands, July, 1990.
- 56. "Cultured Brain Microvessel Endothelial Cell: An <u>In Vitro</u> Model System to Evaluate Strategies for Drug Targeting to the Brain", National Institute on Drug Abuse Technical Review Meeting, Washington, DC, September, 1990.
- 57. "S-Adenosylhomocysteine Hydrolase: A Target for Design of Antiviral Agents", Chemical Pharmacology Symposium, Purdue University, West Lafayette, IN, May, 1991.
- 58. "The Changing World of Drug Discovery: An Academician's Perspective", 1991 Analytical and Physical Chemistry Symposium, The Upjohn Company, Kalamazoo, MI, May, 1991.
- 59. "Cultured Brain Microvessel Endothelial Cells: An In Vitro Model of the Blood Brain Barrier", 1991 World Congress on Cell and Tissue Culture, Anaheim, CA, June, 1991.
- "Physical and Chemical Stability of Protein Pharmaceuticals", Pharmacy World Congress '91, Washington, DC, September, 1991.
- 61. "Computer-Aided Drug Delivery An Overview", International Society of Quantum Biology and Pharmacology Presidents Meeting, Stanford University, September, 1991.
- 62. "Rational Delivery Strategies to Circumvent Physical and Metabolic Barriers to the Oral Absorption of Peptides", Oral Delivery of Peptides - From Theory to Practice, 1991 Capsugel Symposium, New Brunswick, NJ, September, 1991.
- 63. "Cell Culture Systems for Studying Drug Absorption", Symposium entitled, "Facilitating Drug Absorption from the Gastrointestinal Tract", American Association of Pharmaceutial Scientists Meeting, Washington, DC, November,

1991.

- 64. "Designing Peptides and Peptide-Mimetics with Enhanced Blood Brain Barrier Permeabilities", Symposium entitled, "New Concepts in Drug Delivery to the Brain", American Society of Clinical Pharmacology and Therapeutics", Orlando, FL, March, 1992.
- 65. "Cultured Brain Microvessel Endothelial Cells: an *In Vitro* Model of the Blood Brain Barrier", Symposium entitled, "Blood Brain Barrier Transport", Parke-Davis Company, Ann Arbor, MI, May, 1992.
- 66. "The Role of the Pharmaceutical Scientist in Drug Discovery", symposium entitled, "Oral Absorption and Drug Development", Taisho Pharmaceutical Co., Ltd., Tokyo, Japan, June, 1992.
- 67. "The Use of Cultured Intestinal Epithelial Cells to Evaluate Rational Strategies for Enhancing Drug Permeability", Kanazawa University Symposium, Kanazawa, Japan, June, 1992.
- "Cultured Brain Microvessel Endothelial Cells: An In Vitro Model of the Blood Brain Barrier", 1992 World Congress on Cell and Tissue Culture, Washington, DC, June, 1992.
- 69. "Rational Delivery Strategies to Circumvent Physical and Metabolic Barriers in the Oral Absorption of Peptides", 19th International Symposium on Controlled Release of Bioactive Materials, Orlando, FL, July, 1992.
- 70. "Designing Peptides with Enhanced BBB Permeability", Symposium entitled, "Drug Transport to the Brain", Center for Bio-Pharmaceutical Sciences, Leiden University, The Netherlands, October, 1992.
- 71. "Cultured Brain Microvessel Endothelial Cells: An *In Vitro* Model of the Blood Brain Barrier", Symposium entitled, "*In Vitro* Systems for Studying Epithelial and Endothelial Transport and Metabolism: Applications in Pharmacology and Toxicology", Lepetit Research Center, Gerenzono, Italy, October, 1992.
- 72. "Unique Challenges of Formulation of Proteins: Physical and Chemical Instability", Symposium entitled, "Formulation Approaches to Challenging Intravenous Drugs", Johnson & Johnson, New Brunswick, NJ, October, 1992.
- 73. "The Unique Challenges of Developing Products Derived from Biotechnology", 28th Annual Arden House Conference entitled, "Sterile Biotechnology Products: The Science of Protein Characterization, Dosage Form Development and Manufacturing", Harriman, New York, February, 1993.
- 74. "Rational Design of Peptides with Enhanced Membrane Permeability", Symposium entitled, "Prospects and Progress in Drug Design Based on Peptides and Proteins", Keystone Symposium, Taos, New Mexico, March, 1993.
- 75. "Chemical Instability of Proteins in Solution and in Lyophilized Formulations", Symposium entitled, "Protein Formulations and Delivery", American Chemical Society Meeting, Denver, CO, March, 1993.
- 76. "The Use of Cultured Bovine Brain Microvessel Endothelial Cells to Study the Vectorial Transport of Peptides in the Blood Brain Barrier", Workshop entitled, "Vectorial Transport in Cultured Epithelial and Endothelial Cells", European Tissue Culture Society, Newcastle, England, April, 1993.
- 77. "The Use of Cultured Intestinal Epithelial Cells (Caco-2) to Study the Vectorial Transport of Bile Acids", Physiology Society of Great Britain, Leicester, England, April, 1993.
- 78. "S-Adenosylhomocysteine Hydrolase as a Target for the Design of Antiviral Agents", Symposium entitled, "New Chemotherapeutic Approaches to Cancer and Viral Diseases", 1993 CIC Conference, Sherbrooke, Quebec, Canada, May, 1993.
- 79. "Biopharmaceutical Assessment", 35th Annual International Industrial Research Conference, Merrimac, Wisconsin, June. 1993.
- 80. "Rational Strategies to Enhance the Intestinal Permeability of Peptides", 13th American Peptide Symposium, Edmonton, Alberta, Canada, June, 1993.
- 81. "The Use of Cultured Intestinal Epithelial (Caco-2) Cells to Study Drug Transport and Metabolism", 1993 Gordon Research Conference on Drug Metabolism, July, 1993.
- 82. "Rational Approaches to the Design of Inhibitors of S-Adenosylhomocysteine Hydrolase", FASEB Summer Research
 Conference on the "Biochemistry and Pharmacology of S-Adenosylmethionine and Methylation", Copper Mountain,
 Colorado, August, 1993.
- 83. "Key Problems in Peroral Drug Delivery" and "Strategies to Delivery Peptides Across the Blood Brain Barrier",
 International Symposium entitled, "Methods to Overcome Biological Barriers to Drug Delivery", Controlled Release
 Society Meeting, Kuopio, Finland, August, 1993.

- 84. "Rational Strategies for the Design of Peptides with Enhanced Oral Delivery", International Symposium entitled, "Recent Developments in Transdermal and Advanced Drug Delivery", FIP Post Congress Satellite Symposium, Taipei, Taiwan, September, 1993.
- "The Role of the Intestinal Mucosa in Limiting Oral Drug Delivery", NIGMS Workshop entitled, "Oral Drug Delivery: Interface Between Discovery and Development", Herndon, Virginia, December, 1993.
- "The Unique Challenge of Formulation of Protein Drugs: Physical and Chemical Stability", 3rd Interlaken Conference on Advances in Production of Recombinant Proteins, Interlaken, Switzerland, March, 1994.
- 87. "Storage Stability of Protein Drugs", BioPharm Conference '94, San Francisco, CA, June, 1994.
- 88. "Special Bioavailability Problems with Biotechnology-Derived Drugs", Bio-International '94 Conference, Munich, Germany, June, 1994.
- "Chemical Instability of Proteins in Solution and in Lyophilized Formulations", 1994 Colorado Protein Stability Conference, Breckenridge, CO, July, 1994.
- 90. "Application of Cell Culture Systems to Study Drug Transport and Metabolism", XIIth International Congress of Pharmacology, Montreal, Canada, July, 1994.
- "Technologies, Processes and Problems Associated with Oral Delivery of Peptides", Symposium entitled, "Progress
 Toward Drug Delivery of Peptides and Peptidomimetics", American Chemical Society Meeting, Washington, DC,
 August, 1994.
- 92. "Rational Approaches to the Design of Mechanism-Based Inhibitors of S-Adenosylhomocysteine Hydrolase", Eleventh International Round Table of Nucleosides and Nucleotides, Leuven, Belgium, September, 1994.
- 93. "Predicting Chemical Instability of Proteins in Solution and in Lyophilized Formulations", Recovery of Biological Products VII Symposium, San Diego, CA, September, 1994.
- 94. "The Application of Cultured Epithelial Cells (Caco-2) to Evaluate Rational Strategies to Enhance the Intestinal Permeability of Peptides", Workshop entitled, "Physiological Barriers to Drug Delivery", Paris, France, October, 1994.
- 95. "Rational Design to Enhance Membrane Permeability of Peptides", 6th North American Meeting of the International Society for the Study of Xenobiotics, Raleigh, NC, October, 1994.
- "Physical and Chemical Instability of Proteins An Overview", Symposium entitled, "Formulation and Process Challenges
 with Protein Pharmaceuticals", Ninth Annual Meeting of the American Association of Pharmaceutical Scientists, San
 Diego, CA, November, 1994.
- 97. "The Role of P-Glycoprotein in Regulating the BBB Permeability of Peptide Mimetics", 2nd International Symposium on Drug Transport to the Brain, Amsterdam, The Netherlands, February, 1995.
- 98. "Developing In Vitro Models to Predict Human Drug Transport and Metabolism", Keystone Symposia entitled, "Discovery of Therapeutic Agents", Lake Tahoe, CA, March, 1995.
- "Physicochemical and Biological Factors that Influence a Drug's Cellular Permeability by Passive Diffusion", Symposium entitled, "Lipophilicity in Drug Research and Toxicology", Lausanne, Switzerland, March, 1995.
- 100. "Structural Requirements for Intestinal Absorption of Peptide Drugs", Fifth International Symposium on Delivery and Targeting of Peptides, Proteins and Genes, Leiden, The Netherlands, June, 1995.
- 101. "Physicochemical and Biochemical Factors that Influence the Oral Bioavailability of Peptide Mimetics", Fourteenth American Peptide Symposium, Columbus, Ohio, June, 1995.
- 102. "The Structure and Catalytic Mechanism of S-Adenosylhomocysteine Hydrolase", FASEB Summer Research Conference on Biological Methylations, Saxtons River, Vermont, July, 1995.
- "Affecting Drug Absorption", 55th World Congress of Pharmacy and Pharmaceutical Sciences, Stockholm, Sweden, August, 1995.
- 104. "Rational Design of Peptides with Enhanced Membrane Permeability", AFMC International Medicinal Chemistry Symposium, Tokyo, Japan, September, 1995.
- 105. "Rational Strategies to Enhance the Oral Delivery of Peptides", Western Biotech Conference, San Diego, CA, October, 1995.

- 106. "Physical and Chemical Instability of Peptides in Formulations and Drug Delivery System", American Chemical Society Conference on Formulation and Drug Delivery, Boston, MA, October, 1995.
- 107. "Rational Design of Prodrug Strategies to Enhance Membrane Permeability of Peptides", Hoffmann-LaRoche sponsored Wildhaus Scientific Conference, Wildhaus, Switzerland, February, 1996.
- 108. "Use of Intestinal Tissue for Assessing Oral Bioavailability", Western Regional American Association of Pharmaceutical Scientists Meeting, South San Francisco, CA, March, 1996.
- 109. "The Application of Cell Culture Systems to Facilitate the Identification of Drugs with Enhanced Oral Bioavailability", Strategic Research Institute Conference on Lead Generation and Optimization, New Orleans, LA, March, 1996.
- "Chemical Strategies to Overcome Biological Barriers: An Overview", Swedish Academy of Pharmaceutical Sciences
 Mini-Symposium on Drug Delivery by Means of Chemical Modification: Prodrugs-Soft Drugs, Stockholm, Sweden,
 March, 1996.
- 111. "Rational Design of Peptidomimetics with Enhanced Intestinal Mucosal Permeability Properties", Cambridge Healthcare Institute Conference on Development of Small Molecule Mimetic Drugs, Washington, DC, May, 1996.
- 112. "Novel Esterase-Sensitive Cyclic Prodrugs of a Model Hexapeptide Having Enhanced Membrane Permeability and Enzymatic Stability", XIVth International Symposium on Medicinal Chemistry, Maastricht, The Netherlands, September, 1996.
- "Rational Design of Peptides for Intestinal Absorption", 1996 Immobilized Artificial Membrane Meeting, Chicago, IL, September, 1996.
- 114. "Novel Strategies for the Synthesis of Cyclic Peptides with Increased Metabolic Stability and Enhanced Cellular Permeability", MNPC Mini-Symposium, Eleventh Annual Meeting of the American Association of Pharmaceutical Scientists, Seattle, WA, October, 1996.
- 115. "Use of Cultured Bovine Brain Microvessel Endothelial Cells to Elucidate the Structural Features of Peptides that Afford Optimal Permeation of the Blood-Brain Barrier Via Passive Diffusion", Table Ronde Roussel UCLAF #85 entitled, "Passage of Drugs Across Physiological Barriers", Paris, France, December, 1996.
- 116. "Physical and Chemical Instability of Proteins and Peptides in Formulations and Drug Delivery Systems", 1st Symposium on the Analysis of Well Characterized Biotechnology Pharmaceuticals, San Francisco, CA, January, 1997.
- 117. "Membrane Transport as a Barrier to Drug Delivery", 2nd Winter Conference on Bioorganic and Medicinal Chemistry, Steamboat Spring, CO, January, 1997.
- 118. "Use of Cell Culture Models for Understanding and Predicting Oral Drug Absorption", Sixteenth Annual Northeastern Regional Pharmaceutics Association Meeting, Rocky Hill, Connecticut, April, 1997.
- 119. "Prodrug Strategies to Enhance the Permeation of Peptides in the Intestinal Mucosa", The Impact of Pharmacokinetics in Modern Drug Development Symposium, San Francisco, CA, May, 1997.
- 120. "Chemical Instability of Proteins", Biochemical Engineering X Meeting, Kananaskis, Alberta, Canada, May, 1997.
- 121. "Application of the Prodrug Principle to Overcoming Oral Absorption Problems of Peptides", Fourth International Conference on Drug Absorption, Edinburgh, Scotland, June, 1997.
- 122. "Prodrug Strategies to Enhance the Intestinal Mucosa and Blood-Brain Barrier Permeation of Peptides", American Peptide Symposium, Nashville, Tennessee, June, 1997.
- 123. "The Unique Challenges of Stabilizing Therapeutic Peptides and Proteins", American Association of Colleges of Pharmacy Annual Meeting, Indianapolis, IN, July, 1997.
- 124. "Prodrug Strategies to Enhance the Intestinal Mucosa and Blood-Brain Barrier Permeation of Peptides", The Alfred Benzon Symposium entitled Peptide and Protein Drug Delivery, Copenhagen, Denmark, August, 1997.
- 125. "Use of Cell Culture Models as High Throughput Screens for Estimating Oral Drug Absorption", Society for Biomolecular Screening Annual Meeting, San Diego, CA, September, 1997.
- 126. "Optimizing Oral Absorption of Peptides Using Prodrug Strategies", Conference on Formulations and Drug Delivery II, La Jolla, CA, October, 1997.
- 127. "Factors that Determine the Disposition and Activity of Biotechnology Products In Vivo: An Overview", 8th

- International Society for the Study of Xenobiotics Meeting, Hilton Head, SC, October, 1997.
- 128. "Optimizing Oral Absorption of Peptides Using Prodrug Strategies", Conference on Challenges for Drug Delivery and Pharmaceutical Technology, Tokyo, Japan, June, 1998.
- "Optimizing Oral Absorption of Peptides Using Prodrug Strategies", 26th National Medicinal Chemistry Symposium, Richmond, VA, June, 1998.
- "Optimizing Oral Absorption of Peptides Using Prodrug Strategies", 1998 American Association of Colleges of Pharmacy Meeting, Aspen, CO, July, 1998.
- 131. "Permeability Determination and Applications: Industry/Academic Perspective", AAPS Workshop on Permeability Definitions and Regulatory Standards for Bioequivalence, Arlington, VA, August, 1998.
- 132. "The Unique Challenges of Stabilizing Therapeutic Peptides and Proteins to Chemical Degradation", Novo Nordisk 2nd Protein Stability Symposium, Hvidore, Denmark, August, 1998.
- 133. "Bridging the Gaps in Academia in Order to Properly Train Pharmaceutical Scientists for the 21st Century", 1998 American Association of Pharmaceutical Scientists Meeting, San Francisco, CA, November, 1998.
- 134. "Prodrug Strategies to Optimize the Oral Bioavailability of RGD Peptide Mimetics", 9th International Symposium on Recent Advances in Drug Delivery Systems, Salt Lake City, UT, February, 1999.
- 135. "Prodrug Strategies to Improve the Oral Absorption of Peptide Mimetics", Symposium entitled, "Drug Delivery in the 21st Century", 217th American Chemical Society Meeting, Anaheim, CA, March, 1999.
- 136. "Profiling Compounds for Biopharmaceutical Properties: Overview", Symposium entitled, "Biopharmaceutical Profiling", 217th American Chemical Society Meeting, Anaheim, CA, March, 1999.
- 137. "Permeability Determination and Applications: Industry/Academic Perspective", International Symposium entitled, "Strategies for Optimizing Oral Drug Delivery: Scientific to Regulatory Approaches", Kobe, Japan, April, 1999.
- 138. "Lipids, Lipidic Excipients and Enterocyte-Based P-Glycoprotein and Cytochrome P-450-3A4 Mediated Processes", International Symposium entitled, "Recent Advances in the Formulation and Development of Poorly-Soluble Drugs", St. Remy, France, June, 1999.
- 139. "Is the Intestinal Mucosa a Physical or a Biological Barrier to Oral Delivery?", Symposium entitled, "Strategies for Oral Delivery of Challenging Molecules", Merrimac, WI, June, 1999.
- 140. "S-Adenosylmethionine and Methylation: The First 50 Years", FASEB Summer Research Conference on "Biological Methylation", Saxton River, VT, July, 1999.
- 141. "How Structure Influences the Oral Absorption of Peptidemimetics", Smissman Award Symposium, American Chemical Society Annual Meeting, New Orleans, LA, August, 1999.
- 142. "How Structure Influences the Oral Absorption of Peptides", Host-Madsen Award Lecture at the World Congress of Pharmacy and Pharmaceutical Sciences '99, Barcelona, Spain, September, 1999.
- 143. "How Structure Influences Permeation of Drugs Across the Blood-Brain Barrier", Pharma Biotec Center Symposium, Sandbjerg Castle, Denmark, October, 1999.
- 144. "Training Grants in the Chemical and Biological Sciences", workshop entitled "Graduate Education in the Chemical Sciences: Issues for the 21st Century", sponsored by the National Research Council, Washington, DC, December, 1999.
- 145. "Biological Models to Assess Drug Bioavailability", Lipophilicity in Drug Disposition Symposium, University of Lausanne, Lausanne, Switzerland, March, 2000.
- 146. "How Structure Influences the Cell Permeation of Peptides and Peptidemimetics", Plenary Presentation at the Millennial World Congress of Pharmaceutical Sciences, San Francisco, CA, April, 2000.
- 147. "Effect of Lipidic Excipients on Efflux Transporters in the Intestinal Mucosa", Birmingham 2000, British Pharmaceutical Conference, Birmingham, England, August, 2000.
- 148. "How to Design High Affinity Receptor Ligands that Have Drug-like Characteristics", Workshop entitled, "What Makes a Drug Attractive for Its Receptor: ADME, Affinity and Selectivity", Schloss Rauischholzhausen, Marburg, Germany, March, 2001.
- 149. "How Structure Influences the Intestinal Mucosal Permeation of Peptide and Peptidemimetic Drugs", Pharmaceutical

- Congress of the Americas, March, 2001.
- 150. "The Use of Cell Culture Systems as Models of the Intestinal Mucosa in Drug Discovery and Development", World Congress of Pharmacy and Pharmaceutical Sciences 2001, Singapore, September, 2001.
- 151. "The Use of Cell Culture Models to Predict Oral Absorption of Drugs in Humans", International Workshop on the Biopharmaceutics Classification System, London, UK, October, 2001.
- 152. "Role of Cell Culture Models of Biological Barriers in Pharmaceutical R&D", Short Course entitled, "Cell Culture and In Vitro Models for Drug Absorption and Delivery", University of Saarland, Saarbrucken, Germany, February, 2002.
- 153. "Profiling Compounds for Biopharmaceutical Properties: Overview", Symposia entitled "The Role of Bioanalytical Chemists in Profiling the Biopharmaceutical Properties of Drug Candidates", PITTCON 2002, New Orleans, LA, March, 2002.
- 154. "Transport Across the Intestinal mucosa. Are There Lessons for the Blood-Brain Barrier?", Gordon Research Conference entitled, "Barariers of the CNS", Tilton School, Tilton, NH, June, 2002.
- 155. "Drug Design with Biopharmaceutics in Mind", AAPS/FIP/Chinese Pharmaceutical Society Joint Symposium on Scientific and Regulatory Challenges of Pharmaceutical Sciences, Beijing, China, July, 2002.
- 156. "Applications of Cell Culture Models of the Intestinal Mucosa in Drug Discovery and Development", AAPS/FIP/Chinese Pharmaceutical Society Joint Symposium on Scientific and Regulatory Challenges of Pharmaceutical Sciences, Beijing, China, July, 2002.
- "Predictive Models for Permeability-Standard and Novel Techniques", British Pharmaceutical Conference, Manchester, England, September, 2002.
- 158. "Will Cell Culture Models be Predictive of Transporter-Mediated Drug Permeation in the Context of BCS?", AAPS Workshop entitled, "Biopharmaceutical Classification System", Arlington, VA, September, 2002.
- 159. "The Challenges of Designing Cyclic Prodrugs of Opioid Peptides that Permeate the Intestinal Mucosa and the Blood-brain Barrier", 2002 American Association of Pharmaceutical Scientists, Toronto, Canada, November, 2002.
- 160. "Developing Rational Strategies to Stabilize Protein Therapeutics Based on Knowledge About the Protein's Potential Pathways of Chemical Degradation", Short Course entitled, "Analytical Challenges in the Formulation of Pharmaceutical Proteins", Royal Danish School of Pharmacy, Copenhagen, Denmark, December, 2002.
- 161. "Educational and Communication Issues Associated with Integrating and Applying Drug-like Data in Drug Discovery", AAPS Workshop entitled, "Pharmaceutical Profiling in Drug Discovery for Lead Selection", Whippany, NJ, May, 2003.
- 162. "Scientific, Educational and Communication Issues Related to Candidate Selection", 45th Annual Land O'Lakes Conference entitled, "Rational Drug Product Design", Merrimac, WI, June, 2003.
- 163. "Educational and Communication Issues Related to Profiling Compounds for their Drug-like Properties", LogP 2004 Symposium, Zurich, Switzerland, March, 2004.
- 164. "Drug Design with Biopharmaceutics in Mind: A Paradigm Shift in Drug Discovery", European Drug Absorption Network Meeting, Leuven, Belgium, March, 2004.
- B. University or Industry (Since 1975)
 - 1. Department of Pharmacology, School of Pharmacy, University of Wisconsin, Madison, Wisconsin, September, 1975.
 - Department of Pharmacology, School of Medicine, University of Minnesota, Minnesota, Minnesota, November, 1975
 - Department of Medicinal Chemistry, School of Pharmacy, University of Minnesota, Minnesota, November, 1975.
 - Department of Neurology, Mount Sinai School of Medicine, New York, December, 1975.

- 5. Department of Pharmacology, School of Medicine, Yale University, New Haven, Connecticut, December, 1975.
- 6. Burroughs-Wellcome Corporation, Research Triangle Park, North Carolina, June, 1976.
- 7. Department of Pharmacology, Mayo Foundation, School of Medicine, Rochester, Minnesota, July, 1976.
- 8. Lilly Research Laboratories, Indianapolis, Indiana, October, 1976.
- 9. Department of Chemistry, University of Indiana, Bloomington, Indiana, October, 1976.
- 10. Smith Kline & French Laboratories, Philadelphia, Pennsylvania, October, 1976.
- 11. Medical College of Virginia, Department of Pharmacology, Richmond, Virginia, December, 1977.
- 12. The John Curtin School of Medical Research, The Australian National University, Camberra City, Australia, March, 1979.
- 13. Department of Pharmacy, The University of Sydney, Sydney, Australia, March, 1979.
- 14. School of Pharmaceutical Chemistry, Victorian College of Pharmacy, Ltd., Melbourne, Australia, March, 1979.
- 15. School of Pharmaceutics, Victorian College of Pharmacy, Ltd., Melbourne, Australia, March, 1979.
- 16. School of Pharmacy, Oregon State University, Corvallis, Oregon, February, 1979.
- 17. Department of Biochemistry and Biophysics, Oregon State University, Corvallis, Oregon, February, 1979.
- 18. Department of Pharmacology, School of Medicine, Ohio State University, November, 1979.
- 19. E. C. Franklin Lecture, University of Kansas April, 1980.
- 20. School of Pharmacy, University of Wisconsin, June, 1980.
- 21. Department of Pharmacology, University of Nebraska Medical Center, Omaha, Nebraska, September, 1980.
- 22. Department of Chemistry, University of Missouri-Rolla, October, 1980.
- 23. Department of Biochemistry, University of Missouri-Columbia, October, 1980.
- 24. Department of Chemistry, University of Missouri-Kansas City, October, 1980.
- 25. Department of Biochemistry, Kansas State University, Manhattan, Kansas, October, 1980.
- 26. University of Oklahoma, Health Sciences Center, January, 1981.
- 27. Department of Biochemistry, Iowa State University, January, 1981.
- 28. School of Pharmacy, University of Nebraska, Omaha, Nebraska, January, 1981.
- 29. Department of Chemistry, University of Nebraska, Lincoln, Nebraska, January, 1981.
- 30. Department of Biochemistry, University of Kansas Medical Center, Kansas City, Kansas, February, 1981.
- 31. Biology Division, National Cancer Center Research Institute, Tokyo, Japan, April, 1981.
- 32. Sankyo Company, Limited, Tokyo, Japan, April, 1981.
- 33. Department of Biochemistry, National Taiwan University Medical Center, Taipei, Taiwan, April, 1981.
- Department of Pharmaceutical Chemistry, National Taiwan University, School of Pharmacy, Taipei, Taiwan, April, 1981.
- 35. Department of Biochemistry, National Yang Ming Medical College, Taipei, Taiwan, April, 1981.
- 36. Department of Pharmacology, University of Kansas Medical Center, Kansas City, Kansas, December, 1981.
- 37. Allergan Corporation, Irvine, California, January, 1982.

- 38. Burroughs Wellcome Corporation, Research Triangle Park, North Carolina, February, 1982.
- 39. University of Kansas, Summerfield Professorship Inaugural Lecture, April, 1982.
- 40. G. D. Searle Corporation, North Chicago, Illinois, June, 1982.
- 41. Department of Medicinal Chemistry, School of Pharmacy, University of Iowa, Iowa City, Iowa, October, 1982.
- 42. Schering Corporation, Bloomfield, New Jersey, October, 1982.
- 43. The Upjohn Company, Kalamazoo, Michigan, September, 1983.
- 44. School of Pharmacy, University of Michigan, Ann Arbor, Michigan, September, 1983.
- 45. Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania, October, 1983.
- 46. Smith Kline & French Laboratories, Philadelphia, Pennsylvania, October, 1983.
- 47. School of Pharmacy, University of Rhode Island, Kingston, Rhode Island, November, 1983.
- 48. Department of Pharmacology, Medical School of New Jersey, Newark, New Jersey, February, 1984.
- 49. Department of Pharmacology, University of Kansas Medical School, Kansas City, Kansas, February, 1984.
- 50. National Center for Drugs and Biologies, Food and Drug Administration, March, 1984.
- 51. Pfizer Corporation, Groton, Connecticut, September, 1984.
- 52. Schering Corporation, Bloomfield, New Jersey, October, 1984.
- 53. Wichita State University, Wichita, Kansas, November, 1984.
- 54. Upjohn Corporation, Kalamazoo, Michigan, December, 1984.
- 55. Upjohn Corporation, Craveley, England, February, 1985.
- 56. Smith Kline & French Laboratories, Philadelphia, Pennsylvania, March, 1985.
- 57. Ciba-Geigy Corporation, Summit, New Jersey, May, 1985.
- 58. Berlex Laboratories, Cedar Knolls, New Jersey, May, 1985.
- 59. Upjohn Corporation, Kalamazoo, Michigan, October, 1985.
- 60. Walter Reed Army Institute of Research, Washington, DC, October, 1985.
- 61. Laboratory on Oncology Research, Mayo Clinic, Rochester, Minnesota, December, 1985.
- 62. Travenol Laboratories, Inc., Morton Grove, Illinois, January, 1986.
- 63. Bristol-Myers Corporation, Syracuse, New York, February, 1986.
- 64. Burroughs Wellcome, Inc., Research Triangle Park, North Carolina, February, 1986.
- 65. Lederle Laboratories, Pearl River, New York, July, 1986.
- 66. Alcon Laboratories, Fort Worth, Texas, July, 1986.
- 67. G. D. Searle & Co., St. Louis, Missouri, September, 1986.
- 68. Glaxo, Inc., Research Triangle Park, North Carolina, November, 1986.
- 69. Adria Laboratories, Inc., Columbus, Ohio, December, 1986.
- 70. Lilly Research Laboratories, Indianapolis, Indiana, February, 1987.
- 71. G. D. Searle & Co., Chicago, Illinois, February, 1987.

- 72. Northeast Section of the American Chemical Society, Boston, Massachusetts, April, 1987.
- 73. School of Pharmacy, University of Florida, Gainesville, Florida, April, 1987.
- 74. Victorian College of Pharmacy, Ltd, Melbourne, Australia, August, 1987.
- 75. Faulding Research & Development, Adelaide, Australia, August, 1987.
- 76. Syntex Corporation, Palo Alto, California, October, 1987.
- 77. Alza Corporation, Palo Alto, California, October, 1987.
- 78. Johnson & Johnson, New Brunswick, New Jersey, October, 1987.
- 79. Merck Sharp & Dohme, West Point, Pennsylvania, December, 1987.
- 80. Smith Kline & French Laboratories, Philadelphia, Pennsylvania, December, 1987.
- 81. Hoechst, Roussel Pharmaceutical, Inc., Somerville, New Jersey, January, 1988.
- 82. Merck Sharp & Dohme, Rahway, New Jersey, January, 1988.
- 83. Hoshi University, Tokyo, Japan, April, 1988.
- 84. Sankyo Co., Tokyo, Japan, April, 1988.
- 85. Eisai Co., Tokyo, Japan, April, 1988.
- 86. Tokyo University, Tokyo, Japan, April, 1988.
- 87. S-S Pharmaceutical Co., Ltd., Ikebukuro, Japan, April, 1988.
- 88. Josai University, Tokyo, Japan, April, 1988.
- 89. Hokkaido University, Sapporo, Japan, April, 1988.
- 90. Toyo Jozo Co., Ltd., Mishima, Japan, April, 1988.
- 91. Nagoya City University, Nagoya, Japan, April, 1988.
- 92. Takeda Chem. Ind., Ltd., Osaka, Japan, April, 1988.
- 93. Kyoto University, Kyoto, Japan, April, 1988.
- 94. Teikoku Company, Tokushima, Japan, April, 1988.
- 95. Hiroshima University, Hiroshima, Japan, April, 1988.
- 96. Procter & Gamble Company, Norwich, Connecticut, May, 1988.
- 97. Procter & Gamble Company, Cincinnati, Ohio, May, 1988.
- 98. University of Cincinnati, School of Pharmacy, Cincinnati, Ohio, May, 1988.
- 99. Emporia State University, Emporia, Kansas, September, 1988.
- 100. University of Oklahoma, Department of Chemistry, Norman, Oklahoma, October, 1988.
- 101. Rutgers University, Department of Chemistry, Newark, New Jersey, September, 1988.
- 102. Roche Institute of Molecular Biology, Nutley, New Jersey, September, 1988.
- 103. Rutgers University, School of Pharmacy, Piscataway, New Jersey, December, 1988.
- 104. University of Washington, School of Pharmacy, Seattle, Washington, December, 1988.
- 105. Ohio State University, School of Pharmacy, Columbus, Ohio, December, 1988.

- 106. Amgen Corporation, Thousand Oaks, California, January, 1989.
- Brigham Young University, Department of Chemistry, Provo, Utah, January, 1989.
- 108. Glaxo, Inc., Research Triangle Park, North Carolina, February, 1989.
- 109. University of Michigan, School of Pharmacy, Ann Arbor, Michigan, February, 1989.
- 110. Merrell Dow Research Institute, Cincinnati, Ohio, February, 1989.
- 111. University of Kentucky, College of Pharmacy, Lexington, Kentucky, March, 1989.
- 112. University of Minnesota, College of Pharmacy, Minneapolis, Minnesota, April, 1989.
- 113. Hassle Corporation, Goteburg, Sweden, April, 1989.
- 114. Uppsala University, Uppsala, Sweden, April, 1989.
- 115. Alkermes, Inc., Boston, Massachusetts, May, 1989.
- 116. Gensia Pharmaceuticals, Inc., San Diego, California, May, 1989.
- 117. Drug Delivery Systems Institute, Tsukuba, Japan, July, 1989.
- 118. Upjohn--Japan, Tsukuba, Japan, July, 1989.
- 119. Daiichi Pharmaceutical Co., Tokyo, Japan, July, 1989.
- 120. Eisai Pharmaceutical Co., Tsukuba, Japan, July, 1989.
- 121. Yamanouchi Pharmaceutical Co., Tsukuba, Japan, July, 1989.
- 122. Taiho Pharmaceutical Co., Tokushimo, Japan, July, 1989.
- 123. Shionogi Pharmaceutical Co., Osaka, Japan, July, 1989.
- 124. Takeda Chemical Industry, Osaka, Japan, July, 1989.
- 125. Squibb Corporation, Princeton, New Jersey, September, 1989.
- 126. Pfizer Corporation, Groton, Connecticut, September, 1989.
- 127. Univ. of Rhode Island, School of Pharmacy, Kingston, Rhode Island, September, 1989.
- 128. Kansas City Discussion Group of Pharmaceutical and Allied Sciences, Overland Park, Kansas, September, 1989.
- 129. Univ. of New York-Buffalo, School of Pharmacy, Buffalo, New York, October, 1989.
- 130. Grace Cancer Drug Center, Roswell Park Memorial Institute, Buffalo, New York, October, 1989.
- 131. Univ. of Iowa, Dept. of Chemistry, Iowa City, Iowa, October, 1989.
- 132. Univ. of Wisconsin, School of Pharmacy, Madison, Wisconsin, November, 1989.
- 133. Eastman Pharmaceuticals, Inc., Malvern, Pennsylvania, December, 1989.
- 134. Squibb Corporation, Princeton, New Jersey, February, 1990.
- 135. North Jersey Drug Metabolism Discussion Group Meeting, Clifton, NJ, April, 1990.
- 136. University of Toledo, Toledo, Ohio, October, 1990.
- 137. Department of Pharmacology, University of Kansas Medical Center, Kansas City, Kansas, November, 1990.
- 138. Parke-Davis Company, Ann Arbor, Michigan, December, 1990.
- 139. Applied Analytical Systems, Wilmington, North Carolina, January, 1991.

- 140. 3M Pharmaceuticals, Minneapolis, Minnesota, April, 1991.
- 141. The Upjohn Company, Kalamazoo, Michigan, May, 1991.
- 142. Procter & Gamble Company, Cincinnati, Ohio, May, 1991.
- 143. Purdue University, West Lafayette, Indiana, May, 1991.
- 144. University of Arizona, Tucson, Arizona, September, 1991.
- 145. Applied Analytical Systems, Wilmington, North Carolina, September, 1991.
- 146. Gilead Corporation, Forest City, California, September, 1991.
- 147. Baxter Healthcare Corporation, Lincolnshire, Illinois, October, 1991.
- 148. SmithKline Beecham, King of Prussia, Pennsylvania, October, 1991.
- 149. Wichita State University, Wichita, Kansas, November, 1991.
- 150. Howard University, Washington, DC, November, 1991.
- 151. Marion Merrell Dow, Kansas City, Missouri, December, 1991.
- 152. Syntex Research, Palo Alto, California, January, 1992.
- 153. Fisons Pharmaceuticals, Rochester, New York, March, 1992.
- 154. Wichita State University, Wichita, Kansas, April, 1992.
- 155. Abbott Laboratories, North Chicago, Illinois, May, 1992.
- 156. Ciba-Geigy Corporation, Summit, New Jersey, May, 1992.
- 157. Rhone-Poulenc Rorer Pharmaceuticals, Collegeville, Pennsylvania, May, 1992.
- 158. Parke-Davis Company, Ann Arbor, Michigan, May, 1992.
- 159. Upjohn Pharmaceutical Ltd., Tsukuba, Japan, June, 1992.
- 160. Hisamitsu Pharmaceutical Co., Inc., Tsukuba, Japan, June, 1992.
- 161. Eisai Pharmaceutical Co., Tsukuba, Japan, June, 1992.
- 162. Japan Tobacco, Inc., Yokohama, Japan, June, 1992.
- 163. Kanazawa University, Kanazawa, Japan, June, 1992.
- 164. Taisho Pharmaceutical Co., Ltd., Saitama, Japan, June, 1992.
- 165. Shieseido Co., Ltd., Tokyo, Japan, June, 1992.
- 166. Kyusyu University, Fukuoka, Japan, June, 1992.
- 167. Kyoto University, Kyoto, Japan, June, 1992.
- 168. Fujisawa Pharmaceutical Co., Osaka, Japan, June, 1992.
- 169. Takeda Chemical Industry, Osaka, Japan, June, 1992.
- 170. Sandoz Pharmaceutical Corp., East Hanover, New Jersey, September, 1992.
- 171. Johnson and Johnson, New Brunswick, New Jersey, October, 1992.
- 172. DuPont Merck Pharmaceutical Corp., Wilmington, Delaware, November, 1992.
- 173. Merck Sharp & Dohme Research Laboratories, Rahway, NJ, November, 1992.

- 174. St. John's Univ., New York, New York, November, 1992.
- 175. Syntex Corporation, Palo Alto, California, December, 1992.
- 176. Alza Corporation, Palo Alto, California, December, 1992.
- 177. University of Tennessee, Memphis, Tennessee, January, 1993.
- 178. Merck Sharp & Dohme Research Laboratories, Rahway, NJ, February, 1993.
- 179. Merck Sharp & Dohme Research Laboratories, West Point, PA, February, 1993.
- 180. Schering-Plough Research Institute, Kenilworth, NJ, February, 1993.
- 181. University of North Carolina, Chapel Hill, NC, February, 1993.
- 182. Glaxo Inc., Research Triangle Park, NC, February, 1993.
- 183. Chiron, Inc., Emeryville, CA, February, 1993.
- 184. University of Colorado, Denver, CO, April, 1993.
- 185. Southwest Missouri State University, Springfield, MO, April, 1993.
- 186. Ciba-Geigy Pharmaceuticals, Horsham, England, April, 1993.
- 187. Glaxo Research Group, Ware, England, April, 1993.
- 188. SmithKline Beecham, Mundells, England, April, 1993.
- 189. Vertex Pharmaceuticals, Cambridge, MA, May, 1993.
- 190. Bristol-Myers Squibb, Wallingford, CT, May, 1993.
- 191. Rhone Poulenc Rorer Central Research, Collegeville, PA, May, 1993.
- 192. SmithKline Beecham Pharmaceuticals, King of Prussia, PA, May, 1993.
- 193. Abbott Laboratories, North Chicago, IL, June, 1993.
- 194. Wyeth Ayerst Laboratories, Rouses Point, NY, June, 1993.
- 195. Daiichi-Seiyaku Pharmaceutical Co., Tokyo, Japan, September, 1993.
- 196. Hoechst-Japan, Tokyo, Japan, September, 1993.
- 197. National Defense University, Taipei, Taiwan, September, 1993.
- 198. University of California, San Francisco, October, 1993.
- 199. Tanabe Research Laboratories, San Diego, CA, October, 1993.
- 200. Genentech, Inc., South San Francisco, CA, October, 1993.
- 201. University of Missouri, Columbia, MO, November, 1993.
- 202. Glaxo Inc., Research Triangle Park, NC, November, 1993.
- 203. National Institute on Drug Abuse, Rockville, MD, December, 1993.
- 204. University of Michigan, Ann Arbor, MI, March, 1994.
- 205. Sandoz Pharma Ltd., Basel, Switzerland, March, 1994.
- 206. Ciba-Geigy Ltd., Basel, Switzerland, March, 1994.
- 207. Hoffmann-LaRoche, Basel, Switzerland, March, 1994.

- 208. Pharmazeutisches Institute, University of Basel, Basel, Switzerland, March, 1994.
- 209. University of Kentucky, Lexington, KY, April, 1994.
- 210. Alza Corporation, Palo Alto, CA, May, 1994.
- 211. G. D. Searle Pharmaceutical Co., Skokie, IL, June, 1994.
- 212. SmithKline Beecham Pharmaceuticals, King of Prussia, PA, July, 1994.
- 213. Neurobiological Technologies, Richmond, CA, August, 1994.
- 214. SmithKline Beecham Pharmaceuticals, Harlow, England, September, 1994.
- 215. Pfizer Corp., Groton, CT, September, 1994.
- 216. Westfalische Wilhelms Universitat-Münster, Münster, Germany, October, 1994.
- 217. University of Marburg, Marburg, Germany, October, 1994.
- 218. Rhone Poulenc Rorer, Collegeville, PA, October, 1994.
- 219. Wayne State University, Detroit, MI, December, 1994.
- 220. Kansas City Discussion Group of Pharmaceutical and Allied Sciences, Overland Park, KS, December, 1994.
- 221. The Upjohn Company, Kalamazoo, MI, December, 1994.
- 222. Gilead Sciences, Foster City, CA, January, 1995.
- 223. Alza Corporation, Palo Alto, CA, January, 1995.
- 224. Affymax Corporation, Palo Alto, CA, January, 1995.
- 225. University of Pennsylvania, Philadelphia, PA, April, 1995.
- 226. Katholicke University, Leuven, Belgium, May, 1995.
- 227. Royal Danish School of Pharmacy, Copenhagen, Denmark, May, 1995.
- 228. Glaxo Inc., Research Triangle Park, NC, June, 1995.
- 229. Astra Pharmaceuticals, Rochester, NY, June, 1995.
- 230. Houghten Pharmaceuticals, Inc., LaJolla, CA, June, 1995.
- 231. Sandoz Pharma Ltd., Basel, Switzerland, June, 1995.
- 232. Hoffmann-LaRoche, Ltd., Basel, Switzerland, June, 1995.
- 233. Cephalon, Inc., West Chester, PA, July, 1995.
- 234. Genentech, Inc., South San Francisco, CA, August, 1995.
- 235. Astra Arcus AB, Sodertalje, Sweden, August, 1995.
- 236. Astra Draco, Lund, Sweden, August, 1995.
- 237. University of Uppsala, Uppsala, Sweden, August, 1995.
- 238. Hoechst Pharmaceuticals Ltd., Tokyo, Japan, September, 1995.
- 239. Chugai Pharmaceutical Co., Ltd., Tokyo, Japan, September, 1995.
- 240. Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan, September, 1995.
- 241. University of Tokyo, Tokyo, Japan, September, 1995.

- 242. Sankyo Company, Ltd., Tokyo, Japan, September, 1995.
- 243. Upjohn Pharmaceuticals Ltd., Tsukuba, Japan, September, 1995.
- 244. Kyoto University, Kyoto, Japan, September, 1995.
- 245. Sumitomo Pharmaceutical Co., Ltd., Kyoto, Japan, September, 1995.
- 246. Tanabe Pharmaceutical Co., Ltd., Kyoto, Japan, September, 1995.
- 247. Japan Tobacco, Ltd., Kyoto, Japan, September, 1995.
- 248. Ono Pharmaceutical Co., Kyoto, Japan, September, 1995.
- 249. Cambridge Neurosciences, Cambridge, MA, October, 1995.
- 250. Immulogic Pharmaceutical Corp., Cambridge, MA, October, 1995.
- 251. University of Nebraska, Omaha, NE, October, 1995.
- 252. Alza Corporation, Palo Alto, CA, December, 1995.
- 253. Cibus Pharmaceuticals, Inc., Redwood City, CA, March, 1996.
- 254. Pharmacia & Upjohn, Inc., Stockholm, Sweden, March, 1996.
- 255. Cygnus Pharmaceuticals, Redwood City, CA, April, 1996.
- 256. Arris Pharmaceuticals Corp., South San Francisco, CA, April, 1996.
- 257. Adolar Corporation, Malvern, PA, May, 1996.
- 258. Oncogene Science, Uniondale, NY, May, 1996.
- 259. Wyeth-Ayerst Research, Pearl River, NY, October, 1996.
- 260. Pfizer, Inc., Sandwich, England, November, 1996.
- 261. Glycomed-Ligand, Alameda, CA, November, 1996.
- 262. University of Florida, Gainesville, FL, November, 1996.
- 263. Pharmacia & Upjohn, Inc., Stockholm, Sweden, December, 1996.
- 264. Uppsala University, Uppsala, Sweden, December, 1996.
- 265. Inhale Therapeutic Systems, Palo Alto, CA, February, 1997.
- 266. MetaXen, Palo Alto, CA, February, 1997.
- 267. IntraBiotics Pharmaceuticals, Sunneyvale, CA, February, 1997.
- 268. Isis Pharmaceuticals, Carlsbad, CA, March, 1997.
- 269. Hoechst Marion Roussel, Kansas City, MO, March, 1997.
- 270. Zeneca Pharmaceuticals, Wilmington, DE, January, 1997.
- 271. Vertex Pharmaceuticals, Cambridge, MA, April, 1997.
- 272. Biogen, Cambridge, MA, April, 1997.
- 273. Pfizer, Groton, CT, April, 1997.
- 274. Hybridon, Inc., Cambridge, MA, May, 1997.
- 275. Genentech, South San Francisco, CA, May, 1997.

- 276. Zeneca Pharmaceuticals, Manchester, England, June, 1997.
- 277. Sepracor, Inc., Marlborough, MA, September, 1997.
- 278. Tanabe Research Laboratories, San Diego, CA, September, 1997.
- 279. Parke-Davis Research Laboratories, Ann Arbor, MI, October, 1997.
- 280. University of Michigan, Ann Arbor, MI, October, 1997.
- 281. Vertex Pharmaceuticals, Inc., Cambridge, MA, November, 1997.
- 282. Genentech, South San Francisco, CA, November, 1997.
- 283. National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, November, 1997.
- 284. Athena Pharmaceuticals, South San Francisco, CA, November, 1997.
- 285. SmithKline Beecham Pharmaceuticals, Collegeville, PA, December, 1997.
- 286. AnorMed Pharmaceuticals, Vancouver, BC, January, 1998.
- 287. Millennium Pharmaceuticals, Cambridge, MA, March, 1998.
- 288. GeneMedicine, Houston, TX, March, 1998.
- 289. ARIAD Pharmaceuticals, Cambridge, MA, March, 1998.
- 290. Washington State University, Pullman, WA, April, 1998.
- 291. Oregon State University, Corvallis, OR, April, 1998.
- 292. Eli Lilly Research Laboratories, Indianapolis, IN, April, 1998.
- 293. Hoffmann-LaRoche, Nutley, NJ, May, 1998.
- 294. Synaptic Pharmaceutical Corp., Paramus, NJ, May, 1998.
- 295. Takeda Pharmaceutical Co., Osaka, Japan, June, 1998.
- 296. Sumitomo Pharmaceutical Co., Osaka, Japan, June, 1998.
- 297. Ono Pharmaceutical Co., Kyoto, Japan, June, 1998.
- 298. Yamanouchi Pharmaceutical Co., Shizuoka, Japan, June, 1998.
- 299. Daiichi Pharmaceutical Co., Tokyo, Japan, June, 1998.
- 300. Banyu Pharmaceutical Co., Tsukuba, Japan, June, 1998.
- 301. Sankyo Pharmaceutical Co., Tokyo, Japan, June, 1998.
- 302. Chugai Pharmaceutical Co., Tokyo, Japan, June, 1998.
- 303. Taisho Pharmaceutical Co., Saitama, Japan, June, 1998.
- 304. Novo Nordisk A/S, Hvidore, Denmark, August, 1998.
- 305. Novo Nordisk A/S, Maaloev, Denmark, August, 1998.
- 306. Royal Danish School of Pharmacy, Copenhagen, Denmark, August, 1998.
- 307. Zeneca Pharmaceuticals, Ltd., Macclesfield, England, August, 1998.
- 308. Glaxo-Wellcome Pharmaceuticals, Stevenage, England, September, 1998.
- 309. SmithKline Beecham Pharmaceuticals, Harlow, England, September, 1998.

- 310. Ares Advanced Technology, Randolph, MA, September, 1998.
- 311. Coulter Pharmaceuticals, Palo Alto, CA, November, 1998.
- 312. University of Mississippi, University, MI, December, 1998.
- 313. Praecis Pharmaceuticals, Cambridge, MA, December, 1998.
- 314. Agouron Pharmaceuticals, Inc., San Diego, CA, January, 1999.
- 315. Coelacanth, Inc., Princeton, NJ, January, 1999.
- 316. University of Kansas Medical Center (Physiology), Kansas City, KS, January, 1999.
- 317. Virginia Commonwealth University, Richmond, VA, January, 1999.
- 318. University of the Pacific, Stockton, CA, February, 1999.
- 319. Abbott Laboratories, North Chicago, IL, February, 1999.
- 320. Wayne State University, Detroit, MI, February, 1999.
- 321. University of Connecticut, Storrs, CT, March, 1999.
- 322. Boehringer-Ingelheim, Ridgefield, CT, March, 1999.
- 323. The Immune Response Corporation, Carlsbad, CA, March, 1999.
- 324. Hoechst Marion Roussel, Bridgewater, CT, March, 1999.
- 325. University of Minnesota, Minneapolis, MN, April, 1999.
- 326. University of Colorado, Denver, CO, April, 1999.
- 327. Shionogi & Co., Ltd., Osaka, Japan, April, 1999.
- 328. Organon Pharmaceutical Co., Osaka, Japan, April, 1999.
- 329. Fujisawa Pharmaceutical Co., Osaka, Japan, April, 1999.
- 330. Dainippon Pharmaceutical Co., Osaka, Japan, April, 1999.
- 331. Kumamoto University, Kumamoto, Japan, April, 1999.
- 332. University of Illinois-Chicago, IL, May, 1999.
- 333. University of Singapore, Singapore, May, 1999.
- 334. ViroPharm, Inc., Lionville, PA, May, 1999.
- 335. Scios, Inc., Sunnyvale, CA, June, 1999.
- 336. Hoechst Marion Roussel, Romainville, France, June, 1999.
- 337. Millennium Pharmaceuticals, Inc., Cambridge, MA, August, 1999.
- 338. University of Michigan, Ann Arbor, MI, September, 1999.
- 339. Guilford Pharmaceuticals, Baltimore, MD, September, 1999.
- 340. Biogen Corporation, Cambridge, MA, September, 1999.
- 341. Royal Danish School of Pharmacy, Copenhagen, Denmark, October, 1999.
- 342. TEVA Pharmaceutical Industries, Kfar Saba, Israel, October, 1999.
- 343. Bio-Mega-Boehringer Ingelheim, Montreal, Canada, October, 1999.

- 344. Hoffmann-LaRoche Pharmaceutical Co., Nutley, NJ, November, 1999.
- 345. Bristol-Myers Squibb, New Brunswick, NJ, February, 2000.
- 346. ARIAD Pharmaceuticals, Inc., Cambridge, MA, February, 2000.
- 347. University of Missouri-Kansas City, Kansas City, MO, February, 2000.
- 348. Serono Pharmaceutical Research Institute, Geneva, Switzerland, March, 2000.
- 349. Rutgers University, Piscataway, NJ, March, 2000.
- 350. West Pharmaceutical Services, Lionville, PA, March, 2000.
- 351. Monsanto Company, St. Louis, MO, April, 2000.
- 352. Pharmacia & Upjohn, Kalamazoo, MI, April, 2000.
- 353. Schering Plough Corporation, Kenilworth, NJ, May, 2000.
- 354. Genentech Corporation, South San Francisco, CA, May, 2000.
- 355. Pharmacia, Skokie, IL, June, 2000.
- 356. Sugen Corporation, South San Francisco, CA, June, 2000.
- 357. Chiron Corporation, Emeryville, CA, June, 2000.
- 358. Vertex Corporation, Cambridge, MA, August, 2000.
- 359. Pfizer Corporation, Groton, CT, August, 2000.
- 360. Biogen Corporation, Cambridge, MA, August, 2000.
- 361. Wyeth-Ayerst Pharmaceutical Corporation, Princeton, NJ, October, 2000.
- 362. Pfizer Corporation, Ann Arbor, MI, October, 2000.
- 363. University of Basel, Basel, Switzerland, November, 2000.
- 364. Boehringer Ingelheim, Biberach, Germany, November, 2000.
- 365. University of Leiden, Leiden, The Netherlands, November, 2000.
- 366. University of Utrecht, Utrecht, The Netherlands, November, 2000.
- 367. University of California-San Francisco, San Francisco, CA, December, 2000.
- 368. Chiron Corporation, Emeryville, CA, December, 2000.
- 369. Hoffmann-LaRoche, Palo Alto, CA, December, 2000.
- 370. Genetic Institute, Cambridge, MA, December, 2000.
- 371. University of South Carolina, Charleston, SC, February, 2001.
- 372. Albany Molecular Research Institute, Albany, NY, April, 2001.
- 373. University of Nebraska Medical Center, Omaha, NE, April, 2001.
- 374. New England Drug Metabolism Discussion Group, Cambridge, MA, April, 2001.
- Kansas City Discussion Group of the American Association of Pharmaceutical Scientists, Kansas City, MO, April, 2001.
- 376. Pharmacopeia, Inc., Monmouth Junction, NJ, May, 2001.
- 377. Ricerca, Painesville, OH, May, 2001.

- 378. Roche Bioscience, Inc., Palo Alto, CA, May, 2001.
- 379. Transform Pharmaceuticals, Inc., Boston, MA, June, 2001.
- 380. ArQule Pharmaceuticals, Inc., Boston, MA, June, 2001.
- 381. University of Southern California, Los Angeles, CA, August, 2001.
- 382. Inhale Therapeutics, Inc., San Carlos, CA, October, 2001.
- 383. Aventis, Inc., Bridgewater, NJ, October, 2001.
- 384. Sepracor, Inc., Marlboro, MA, October, 2001.
- 385. Serono, Inc., Boston, MA, October, 2001.
- 386. MetaPhore Pharmaceuticals, Inc., St. Lous, MO, November, 2001.
- 387. Indianapolis/Cincinnati Discussion Group, Indianapolis, IN, November, 2001.
- 388. University of Manchester, Manchester, England, December, 2001.
- 389. Roche Biosciences, Palo Alto, CA, December, 2001.
- 390. Versicor, Fremont, CA, December, 2001.
- 391. Lexicon Pharmaceuticals, Princeton, NJ, January, 2002.
- Department of Pharmacology & Toxicology, The University of Kansas Medical Center, Kansas City, KS, February, 2002.
- 393. Saarland University, Saarland, Germany, February, 2002.
- 394. Immunex, Seattle, WA, March, 2002.
- 395. GlaxoSmithKline, Collegeville, PA, March, 2002.
- 396. AAPS ChicagoLand Discussion Group, May, 2002.
- 397. Baxter Healthcare Corporation, Round Lake, IL, May, 2002.
- 398. Roche Bioscience, Palo Alto, CA, May, 2002.
- 399. Arradial, Inc., Bedford, MA, July, 2002.
- 400. Alkermes, Inc., Cambridge, MA, July, 2002.
- 401. Peking University, Beijing, China, July, 2002.
- 402. Boehringer-Ingelheim, Montreal, Canada, September, 2002.
- 403. Enzon, Inc., Bridgewater, NJ, September, 2002.
- 404. Abbott Laboratories, Chicago, IL, October, 2002.
- 405. Infinity Pharmaceuticals, Cambridge, MA, October, 2002.
- 406. 3D Pharmaceuticals, Exton, PA, November, 2002.
- 407. Royal Danish School of Pharmacy, December, 2002.
- 408. Abbott Laboratories, Ludwingshafen, Germany, December, 2002.
- 409. University of Vienna, Vienna, Austria, December, 2002.
- 410. Aventis, Frankfurt, Germany, December, 2002.

- 411. American Chemical Society Northeastern Section Symposium, December, 2002.
- 412. Achillion Pharmaceuticals, New Haven, CT, December, 2002.
- 413. Sunesis Pharmaceuticals, Inc., South San Francisco, CA, January, 2003.
- 414. University of Pittsburgh, Pittsburgh, PA, February, 2003.
- 415. Rib-X Pharmaceuticals, New Haven, CT, February, 2003.
- 416. Serono, Rockland, MA, February, 2003.
- 417. Synaptic Pharmaceuticals, Paramus, NJ, February, 2003.
- 418. Enzon, Inc., Bridgewater, NJ, February, 2003.
- 419. AstraZeneca, Waltham, MA, March, 2003.
- 420. Bay Area ADME Discussion Group, South San Francisco, CA, May, 2003.
- 421. Purdue Pharma, Cranbury, NJ, July, 2003.
- 422. Rib-X Pharmaceuticals, New Haven, CT, July, 2003.
- 423. Abbott Laboratories, North Chicago, IL, September, 2003.
- 424. North Carolina Drug Metabolism Discussion Group, Chapel Hill, NC, September, 2003.
- 425. 3-D Pharmaceuticals, Exton, PA, October, 2003.
- 426. Rib-X Pharmaceuticals, New Haven, CT, October, 2003.
- 427. Lundbeck Pharmaceuticals, Copenhagen, Denmark, November, 2003.
- 428. Aventis Pharmaceuticals, Frankfurt, Germany, November, 2003.
- 429. Serono, Rockland, MA, December, 2003.
- 430. Synaptic Pharmaceuticals, Paramus, NJ, December, 2003.
- 431. Neurocrine Biosciences Inc., San Diego, CA, December, 2003.
- 432. Pfizer, Ann Arbor, MI, December, 2003.
- 433. Florida International University, Miami, FL, February, 2004.
- 434. Merck Research Laboratories, West Point, PA, February, 2004.
- 435. Aventis Pharmaceuticals, Paris, France, March, 2004.
- 436. Lilly Development Center, Mont-Saint-Guibert, Belgium, April, 2004.
- 437. University of New York-Buffalo, Buffalo, NY, April, 2004.
- 438. Pharmacopeia, Cranbury, NJ, April, 2004.